# Musculoskeletal Infections

## A Clinical Case Book

Julie Reznicek
Paul W. Perdue, Jr.
Gonzalo Bearman
*Editors*

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ISBN 978-3-030-41149-7 ISBN 978-3-030-41150-3 (eBook)
https://doi.org/10.1007/978-3-030-41150-3

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# Preface

With increased specialization in medicine, the unique niche of musculoskeletal infections now exists. Herein, we present 20 cases of relevant and challenging diagnostic and management issues in musculoskeletal infectious diseases, with an emphasis on clinical pearls and medical-surgical collaboration.

We dedicate this book to all the patients and mentors who teach us and advance the practice of medicine.

Richmond, VA, USA

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# Chapter 1
# Presurgical Staphylococcal Decolonization for Select Orthopedic Surgeries

**Michelle Doll and Gonzalo Bearman**

## Case Presentation

A 58-year-old male, with a history of Type 2 diabetes mellitus, daily ½ pack per day cigarette smoking, obesity (BMI 30), and osteoarthritis, presents to an orthopedic clinic for evaluation for a right total knee arthroplasty (TKA). He is tentatively offered the procedure but instructed to optimize diabetes control and quit smoking prior to scheduling of the surgery. Over the next 3 months, he succeeds in bringing his HbA1c from 8.2% to 7.3% and stops smoking. He is found to be methicillin-resistant *Staphylococcus aureus* (MRSA) colonized on a screening swab of nares. The patient undergoes a staphylococcal decolonization protocol consisting of chlorhexidine 2% solution for daily bathing with mupirocin 2% nasal ointment twice daily and chlorhexidine 0.12% oral rinse twice daily, all performed for 5 days prior to his scheduled total knee arthroplasty. He receives intravenous vancomycin as his surgical antibiotic prophylaxis, appropriately dosed for his weight.

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J. Reznicek et al. (eds.), *Musculoskeletal Infections*,
https://doi.org/10.1007/978-3-030-41150-3_1

Unfortunately, his postoperative course is complicated by persistent drainage from the wound, and a joint aspirate culture within 30 days of his operative procedure reveals methicillin-sensitive *Staphylococcus aureus* (MSSA).

## Discussion

Surgical site infections (SSIs) are driven by both modifiable and non-modifiable risk factors. This patient and his surgical team went to great lengths in attempts to optimize his risk for total knee arthroplasty. Of the organisms implicated in prosthetic joint infections, *Staphylococcus aureus* is one of the most common and the most persistent bacterial pathogens [1]. *Staphylococcus* species readily form biofilms on these prosthetic materials [2] and tend to recur after revisions despite explant, debridement, and prolonged courses of antibiotics.

Staphylococcal decolonization prior to surgery with protocols containing chlorhexidine bathing and mupirocin nasal ointment are associated with decreased SSI in surgical patients, particularly in those undergoing elective orthopedic surgeries [3–5]. A summary of these studies is provided in Table 1.1. There are two distinct approaches to staphylococcal decolonization: targeted or universal. A targeted approach uses screening for MRSA or *Staphylococcus aureus* (MRSA and MSSA) and provides the decolonization protocol only for those patients found to be positive for these organisms on nasal swab. Limitations to this method are false-negative nasal swabs or presence of *Staphylococcus aureus* at sites other than the nose that may be missed in nasal screening [6]. In contrast, a universal approach provides decolonization protocols to all preoperative patients regardless of screening. Theoretical drawbacks to this method are overuse of chlorhexidine or mupirocin products with potential production of resistance [7]. Data favoring a universal approach is strongest in the ICU population; a multicenter, randomized clinical trial found significant reductions in all-cause central line-associated infections as well as MRSA bloodstream infection when patients underwent universal decolonization

Table 1.1 Summary of key studies for presurgical decolonization

| Study | Comment |
|---|---|
| Bode et al. [3] | Double-blind randomized controlled multicenter trial in which staphylococcal carriers were either decolonized with nasal mupirocin and chlorhexidine soap or given placebo treatment. Staphylococcal SSIs occurred in 17 of 504 decolonized patients (rate 3.4%) and 32 of 413 placebo patients (rate 7.7%) |
| Rao et al. [4] | Historical control of 741 patients was compared to 1440 intervention patients who underwent screening and targeted decolonization with nasal mupirocin and chlorhexidine soap ($N = 321$). SSI rates fell from 20/741 (rate 2.7%) to 17/1440 (rate 1.2%)<br>The study also prospectively compared the 321 colonized patients to a "concurrent control" of those patients not participating in the screening/decolonization program who might have been colonized and went on to develop staphylococcal SSI; none of the 321 patients developed staphylococcal SSI through the 2-year follow-up |
| Kim et al. [5] | Targeted decolonization with nasal mupirocin and chlorhexidine soap initiated for all elective primary total joint replacements and SSI rates compared against a historical control. SSI occurred in 13/7019 (0.19%) during selective decolonization time period and 24/5293 (0.45%) during pre-intervention period |
| Stambough et al. [9] | *Universal versus targeted decolonization*<br>Targeted decolonization program for elective joint replacements 2011–2013 was compared to universal decolonization program 2013–2015, both using nasal mupirocin and chlorhexidine soap. Over 4000 patients were included over the 4 years, 15 (or 0.8%) had SSI in the selective intervention group, and 5 had SSI in the universal intervention group. Staphylococcal specific SSI also reduced 10 to 2 |

compared to the group randomized to a targeted intervention [8]. Universal decolonization has been evaluated in the total joint arthroplasty patient population with promising results as well, albeit with small-scale observational studies [9].

It is important to note that decolonization procedures may not completely eradicate the organism from a patient. The overall goal is to reduce the bioburden of staphylococci and other skin flora immediately prior to the operative procedure when the patient is at greatest risk of infection. One study documented that up to 20% of patients may remain colonized despite completing 5 days of chlorhexidine 4% body wash and mupirocin 2% nasal ointment [10]. The study was not powered to detect a difference in incidence of SSI. Yet, if patients did complete the protocol, they presumably had decreased bioburden on their skin at the time of operation. A successful decolonization program requires education for both providers and patients as to the rationale and importance of the decolonization procedures [11]. Patient adherence to the protocol should be actively tracked and reported to key stakeholders in order to obtain the desired impact. Instructions to patients must be clearly stated in written form for reference at home. An example of a patient instruction and tracking sheet is shown in Fig. 1.1.

**Preparing for Surgery: Start the instructions below 5 days before your surgery day**

| Activity | Completed | | | | | |
|---|---|---|---|---|---|---|
| Date: | Day1 __/__/__ | Day2 __/__/__ | Day3 __/__/__ | Day4 __/__/__ | Day5 __/__/__ | Day6 __/__/__ |
| **1. Mupirocin 2% ointment**<br>a. Apply two times a day<br>b. Use two Q tips – one for each nostril<br>c. Apply ointment to the inside of each nostril, using a fresh Q-tip for each nostril.<br>d. Do this starting five days before surgery and including the morning of surgery (day 6) | ☐ Morning ☐ Evening | ☐ Morning ☐ Evening | ☐ Morning ☐ Evening | ☐ Morning ☐ Evening | ☐ Morning ☐ Evening | ☐ Day of surgery |
| **2. Peridex (chlorhexidine gluconate) 0.12% mouth rinse:**<br>a. Brush teeth; rinse out all toothpaste with water. *If you wear dentures/partials, take them out and rinse with Peridex.* ***DO NOT SOAK IN PERIDEX.***<br>b. Swish one tablespoonful (15 ml, this is usually the capful) around in the mouth and all teeth for 30 seconds - use a timer for this - then spit out.<br>c. Do not swallow the rinse, although swallowing some leftover medication is fine.<br>d. Do not eat for at least two hours after rinsing<br>e. Do this starting five days before surgery and including the morning of surgery (day 6) | ☐ Morning ☐ Evening | ☐ Morning ☐ Evening | ☐ Morning ☐ Evening | ☐ Morning ☐ Evening | ☐ Morning ☐ Evening | ☐ Day of surgery |
| **3. Chlorhexidine 2% shower or bath soap:**<br>a. Shower or bathe each day starting five days prior to surgery (six showers total). *Test small area on your hand* ***prior*** *to use for any allergic reaction.*<br>b. Use the special soap in the shower just like normal soap, (avoid eyes, ears, and mouth)<br>i. Turn off water in the shower and rub special soap over all skin, especially where the surgical site will be, for at least three minutes<br>ii. Rinse with water, pat dry with a clean towel<br>iii. Do this starting five days before surgery and including the morning of surgery (day 6)<br>iv. Dress in clean clothes | ☐ Daily | ☐ Daily | ☐ Daily | ☐ Daily | ☐ Daily | ☐ Day of surgery |

**Please bring this form with you the day of surgery.**

Rev. 02/2014

FIGURE 1.1 Figure provided by the Department of Infection Prevention, Control, and Epidemiology; Virginia Commonwealth University Health System

Mupirocin is the most widely used agent for nasal decolonization and the agent for which the strongest supportive data currently exists [6, 12]. Alternate nasal decolonization agents include bacitracin, povidone-iodine, and alcohol, with many novel agents in active investigation [6]. Topical body wash has been performed typically with chlorhexidine either 2% or 4% solutions. Triclosan and povidone-iodine have also been used, but concerns regarding toxicity and short duration of action, respectively, limit their utility in decolonization protocols [6]. Dilute bleach baths decrease *Staphylococcus* carriage in persons with chronic skin and soft tissue infection [6]. However, the logistics of mixing and taking the bath limit its inclusion in most preoperative decolonization protocols.

Guidelines for systemic antimicrobial prophylaxis before surgery identify cefazolin as the drug of choice for orthopedic surgery including joint replacement [13]. Cefazolin is an optimal choice given its rapid bactericidal action, low cost, and favorable toxicity profile, as well as the extensive experience with cefazolin for surgical prophylaxis. For those who are penicillin allergic, vancomycin and clindamycin are recommended as alternatives [13]. Both of these agents have weaknesses. Clindamycin is considered bacteriostatic and carries a greater risk of staphylococcal resistance [14]. Vancomycin has a large volume of distribution which can vary substantially between patients [14]. Therefore, it is recommended that vancomycin be given 60–120 minutes prior to surgical incision [13]. In practice, this is often difficult for surgical programs to achieve.

MRSA screening is useful for determining optimal surgical prophylactic antibiotics even in centers using universal decolonization procedures. As noted above, the decolonization procedure cannot be assumed to result in 100% eradication of *Staphylococcus*. Thus for high-risk procedures, such as those involving implants, screening for MRSA allows addition of vancomycin to the surgical prophylaxis regimen. It should be emphasized that guidelines call for the addition of vancomycin to cefazolin, rather than the replacement of cefazolin with vancomycin [13]. It has been noted that patients receiving vancomycin instead of cefazolin are at an

increased risk for MSSA infection [15], likely due to more favorable pharmacokinetics of the cefazolin for sensitive organisms as well as potential problems in the timing of vancomycin administration. Cotogni et al. [16] recently showed that if the vancomycin is still infusing at the time of surgical incision, risk for SSI is increased in both high- and low-risk cardiac surgery patients [16].

*Staphylococcus aureus* infection remains a dreaded postoperative complication of prosthetic joint infection, contributing to significant patient morbidity and excess financial costs. Universal staphylococcal decolonization protocols, MRSA screening, and optimization of surgical prophylaxis have become key interventions to reduce operative risk; the ongoing challenge for surgical teams is to operationalize these interventions and deliver them with high fidelity.

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# Chapter 2
# Prosthetic Joint Infection

**Caitlin P. Oravec and Douglas R. Osmon**

## Case

A 69-year-old male with a past medical history of psoriatic arthritis on methotrexate and right total knee arthroplasty (TKA) complicated by prosthetic joint infection (PJI) is referred to the clinic for swelling and pain in the right knee.

Poor wound healing complicated the primary right TKA, and he developed a PJI on two separate occasions, first with *Escherichia coli* and then with methicillin-sensitive *Staphylococcus aureus*. For each of these PJIs, he underwent a two-stage exchange after a failed DAIR (debridement, antibiotics, and implant retention) procedure. After the second two-stage exchange, PJI recurred with *E. coli*. He underwent another DAIR with placement of antibiotic impregnated calcium sulfate beads and was put on chronic antimicrobial suppression with levofloxacin. He achieved suppression for some time but subsequently developed a draining sinus tract along the incision and, due to increasing pain and swelling, was referred to a specialty center.

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J. Reznicek et al. (eds.), *Musculoskeletal Infections*,
https://doi.org/10.1007/978-3-030-41150-3_2

***Physical Examination*** Vital signs within normal limits. *Skin*: Incision over the right knee intact. Fluid-filled collection at the proximal portion of the incision with serous drainage (Fig. 2.1a). No psoriatic plaques. *Musculoskeletal*: Antalgic gait favoring the right leg. Painful active range of motion 60 degrees to 95 degrees with passive range of motion to 25 degrees. Strength and sensation intact. 2+ PT and DP pulses.

***Laboratory/Radiographic Findings*** White blood cell count 6000 μL, C-reactive protein (CRP) 69.5 mg/L, erythrocyte sedimentation rate (ESR) 67 mm/1 hour. *Right knee synovial fluid*: Bloody, 59,941 total nucleated cells, 96% neutrophils, negative crystal examination. Aerobic culture revealed *Streptococcus mitis* group susceptible to penicillin, ceftriaxone, daptomycin, and vancomycin and resistant to levofloxacin. *X-ray of right knee, lateral view* (Fig. 2.1b): Stemmed femoral and tibial components, with metaphyseal sleeve on the tibial side. Components appear well-fixed without evidence of loosening or wear.

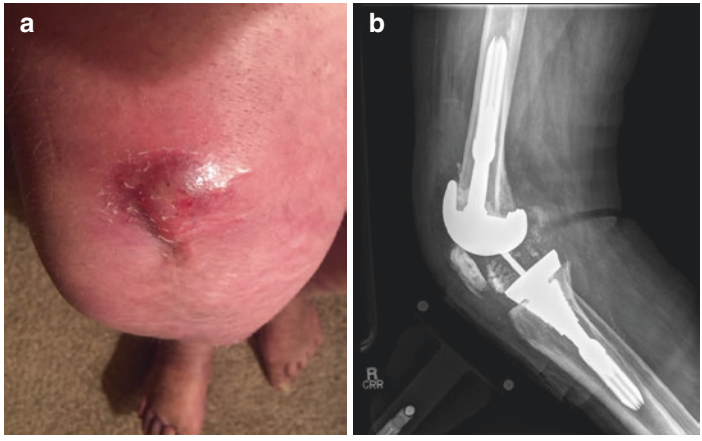


FIGURE 2.1 (**a**) Swelling and sinus tract formation over the proximal surgical incision (**b**) Right knee lateral radiograph

## Discussion

The diagnosis, management, and prevention of a PJI requires a multidisciplinary team of providers including orthopedic and plastic surgeons, infectious disease providers, and microbiologists, along with other experts such as lymphedema, diabetes, and wound care specialists. Early PJI is most often defined as infection that occurs within 0–3 months of implantation [1, 2]. Early PJI can be acquired during surgery (most common), develop secondary to delayed wound healing, or less likely occur via a hematogenous route. Early infection can be monomicrobial with a virulent organism such as *S. aureus* or polymicrobial either as a result of contiguous spread from the surgical incision or inoculation of multiple microorganisms at the time of device implantation [3]. Delayed PJI can present several months to years after prosthesis implantation, is believed to be acquired during prosthesis implantation, and is often due to less virulent organisms [1]. Late infection, presenting several years or more after the index surgery, can be acute as the result of hematogenous seeding from another site of infection or chronic, due to a more indolent organism acquired at the time of surgery [3].

PJI presentation varies based on the mechanism and timing of infection. Early PJI can present with erythema, edema, warmth, tenderness, or persistent wound drainage. Delayed PJI often presents with persistent joint pain in the abscence of other symptoms. Late PJI, if acute, presents as a typical acute septic arthritis syndrome similar to early PJI. Chronic, late PJI often presents with a painful loose prosthesis, particularly in the absence of a pain-free interval after surgery. Chronic infections may also present with development of a sinus tract. Often, there is a history of prior wound healing issues [1, 2].

There is no gold standard for the definition of a PJI. The diagnosis can occur in the preoperative or intraoperative period. Preoperative evaluation should include an ESR, CRP, and plan radiograph of the joint to assess for loosening of the implant. The most widely used definitions of a PJI using multiple pieces of patient information are included in Table 2.1.

Table 2.1 Proposed definitions of prosthetic joint infection [1, 6, 7]

| Organization | Definition |
|---|---|
| IDSA, 2013 | *PJI is present when one of the following criteria is present*<br>Sinus tract communicating with prosthesis<br>Presence of periprosthetic purulence without other etiology<br>Acute inflammation on histopathologic evaluation of periprosthetic tissue<br>Two or more positive cultures with the same organism (intraoperatively and/or preoperatively)<br>Single positive culture with virulent organism |
| MSIS, 2011 | *PJI is present when one major criterion is present or four out of six minor criteria exist*<br>Major criteria<br>A pathogen is isolated by culture from at least two separate tissue or fluid samples obtained from the affected prosthetic joint<br>A sinus tract communicating with the prosthesis<br>Minor criteria<br>Elevated CRP and ESR<br>Elevated synovial leukocyte count<br>Elevated synovial neutrophil percentage (PMN%)<br>Presence of purulence in the affected joint<br>Greater than five neutrophils per high-power field observed from histologic analysis or periprosthetic tissue at x400 magnification<br>Isolation of a microorganism in one culture of periprosthetic tissue or fluid |
| ICM, 2013 | *PJI is present when one major criterion is present or three out of five minor criteria exist*<br>Major criteria<br>Two positive periprosthetic cultures with phenotypically identical organisms<br>A sinus tract communicating with the joint<br>Minor criteria<br>Elevated CRP and ESR<br>Elevated synovial fluid WBC count or ++ change on leukocyte esterase test strip<br>Elevated synovial fluid PMN%<br>Positive histologic analysis of periprosthetic tissue<br>A single positive culture |

The most recent proposed definition takes into account similar criteria to the definitions found in Table 2.1, but also includes additional serum and synovial fluid markers such as D-dimer and alpha-defensin [4]. The use of other serum biomarkers such as procalcitonin, interleukin-6, and tumor necrosis factor, among others, has also been evaluated by researchers. The utility and cost-effectiveness compared to more commonly available tests of these new biomarkers are not clear at this time, but the use of serum D-dimer has recently showed promise, though more research is needed [5]. If there is concern for a PJI due to a hematogenous source or secondary bacteremia due to a PJI, blood cultures should also be obtained. Arthrocentesis should be performed to confirm the diagnosis of a PJI and to identify the pathogen causing a PJI prior to surgical intervention when possible. Synovial fluid evaluation should include a cell count with differential and crystal examination. Synovial fluid alpha-defensin has also been proposed to be an excellent marker of PJI, has been recently FDA approved, but does not define the microbiology of a PJI [2, 4]. The synovial fluid leukocyte count and percent of neutrophils that are associated with a PJI varies and is typically much lower than with native joint septic arthritis [4]. Values that correlate with a PJI have been proposed by the Infectious Diseases Society of America (IDSA), the Musculoskeletal Infection Society (MSIS), and the International Consensus Meeting (ICM) on Prosthetic Joint Infection [1, 6, 7]. Aerobic and anaerobic cultures should also be requested on synovial fluid. Synovial fluid fungal and mycobacterial cultures should be requested if there is concern based on the exposure history or other host factors. Cultures ideally should be obtained when the patient has been off of antibiotics for at least 2 weeks to increase culture yield if the patient's condition allows it [1].

Intraoperative inspection by the surgeon, pathologic examination of periprosthetic tissue for acute inflammation, and periprosthetic tissue cultures can be used to diagnose

PJI. It is recommended to obtain 3–6 periprosthetic tissue and/or fluid samples for culture depending on how cultures are processed in the laboratory. When a prosthesis or its' mobile parts (polyethylene liners, modular components) are resected or exchanged, they can be sent for culture with ultrasonication. Culture of liquid media bathing the prosthesis after ultrasonication can improve culture yield as well as decrease the time to bacterial isolation, identification, and susceptibility testing [3]. Periprosthetic tissue culture in blood culture bottles, in addition to culture of liquid media bathing the prosthesis after ultrasonication, may have the highest yield [8].

Factors that should be taken into consideration when evaluating surgical management strategies for a patient with a PJI involving the hip or knee include duration of symptoms, age and stability of the implant, past surgical interventions, causative organism and susceptibility pattern, comorbidities, availability of resources for management, and more. Debridement, antibiotic, and implant retention (DAIR) with exchange of mobile parts should be considered if the prosthesis is well-fixed, if there is no sinus tract, and if the patient is within 30 days of prosthesis implantation or has had fewer than 3 weeks of symptoms. If a DAIR procedure is done outside these parameters, the risk of relapse is higher [1]. Additional factors that may make the risk of relapse higher after a DAIR procedure include host immune status, the number of prior irrigation and debridements performed, the use of nicotine, and organism sensitivity [9]. A two-stage exchange consists of one surgery to remove the infected components, a course of parenteral antibiotic therapy, and an antibiotic-free period to observe for recrudescence of infection, followed by reimplant of a new prosthesis. After removal of the infected hip or knee prosthesis, a temporary spacer made of antibiotic impregnated polymethylmethacrylate (PMMA) cement is often placed to control the dead space and allow local antimicrobial delivery. These spacers can be articulating so that the patient can be partially weight bearing

or non-articulating if the anatomy will not allow for placement of an articulating spacer. Resection without spacer placement may be done if the organism is deemed exceptionally difficult to treat such as in the case of fungal or mycobacterial infection [3]. A one-stage or direct exchange, while not currently performed commonly in the United States, consists of removal of prosthetic components, debridement, and implantation of new prosthesis with or without using antibiotic cement to fixate the new prosthesis. It can be used in patients who may not be candidates for two surgeries due to medical or surgical comorbidities. Some recent studies show similar success rates to two-stage exchanges with a heavy focus on intraoperative technique and suggest the indications for one-stage exchange to be expanded in the near future [10]. Finally, in patients who are not candidates for the above procedures, permanent resection arthroplasty, arthrodesis, or amputation should be pursued. If amputation is considered, a second opinion at a specialty center is recommended if the patient's condition allows it [1].

Antimicrobials play a key role in treatment of a PJI and work as an adjunct to surgical debridement. Rarely are antibiotics utilized without a surgical debridement [3]. Antibiotics have a role both locally and systemically. Local antibiotics can be used in high doses to fashion cement spacers after a resection arthroplasty, to create absorbable (calcium sulfate) or nonabsorbable (PMMA) beads, or at lower doses in the fixation bone cement when a new implant is placed. One of the benefits of local antibiotic delivery compared to systemic therapy is achievement of higher concentrations and better penetration into tissue that is locally devascularized from surgery and infection, thus resulting in potentially more effective therapy [11]. It has previously been reported that systemic absorption of local antimicrobials after knee resection and placement of antibiotic spacer is often negligible or not clinically significant [12]. Because of case reports of nephrotoxicity in patients with antibiotic-loaded PMMA cement spacers, a recent study sought to quantify those at risk of acute kidney

injury (AKI) after placement of an antibiotic-impregnated cement spacer (ACS). There was no clear association to the specific patient population at higher risk of AKI or kidney failure with an ACS in place [13]. More studies are needed to define the incidence and risk factors of AKI after spacer placement, but it seems reasonable that patients should be monitored for nephrotoxicity, especially if spacers contain high-dose antimicrobials and have a large surface area, drains are not used in the initial postoperative period, the patient has preexisting underlying chronic kidney disease (CKD) or other comorbidities, and medications that can potentiate or cause AKI are being administered concurrently.

The duration of systemic antibiotics varies based on the surgical management strategy but usually includes a 2–6-week period of parenteral therapy for bacteria assuming no concomitant bloodstream infection. If the patient has undergone resection of the infected implants, a course of parenteral therapy is usually sufficient. In a one-stage exchange or DAIR procedure, there may be a period of oral antibiotics after completion of IV antibiotics for antimicrobial suppression, although this practice is highly variable and no high-level evidence exists to guide clinicians in this practice. The duration of oral antibiotics varies widely from several months to chronic suppression for the life of the prosthesis. Suppression is used most often in cases where previous implants are retained, the infecting organism is known to be biofilm producing, or failure to suppress the PJI can lead to catastrophic outcomes such as amputation. The two most common causes of PJI, *S. aureus* and coagulase-negative staphylococci, are excellent at producing biofilm and make up more than 50% of PJI cases. During the initial treatment phase of a staphylococcal PJI when an infected implant is retained, rifampin combination therapy should be used for biofilm penetration if the organism is rifampin susceptible. The current IDSA PJI guidelines rec-

ommend rifampin, in combination with a companion oral drug, to be utilized for 6 months for total knee arthroplasty (TKA) and 3 months for other joints. PJIs caused by fungi or mycobacteria are usually treated for longer periods of time, up to 1 year [1].

Many current clinical and research initiatives will impact the future of PJI diagnosis and management. Some of these include the creation and use of algorithms to guide clinicians in the diagnosis and management of PJI, molecular methods including metagenomics to define the microbiology of infection [14], the role of oral antimicrobials in the medical management of PJI [15], phage therapy's role in the treatment of PJI [16], the use of extended oral antibiotic prophylaxis after two-stage exchange procedures [17], and the role of other rifamycins including rifabutin or rifapentine instead of rifampin for combination therapy after DAIR [18].

Case resolution: There was consideration in this patient for above-the-knee amputation, permanent resection arthroplasty, or arthrodesis. Ultimately, the orthopedic surgeon determined that the patient's level of bone stock was adequate for a third and final attempt at two-stage exchange, which was recommended due to his level of activity and chronicity of symptoms with an understanding that the risk of failure was high. He underwent resection arthroplasty, placement of a non-articulating, static, antibiotic spacer containing vancomycin and gentamicin. He completed a 6-week course of IV ceftriaxone. Intraoperative cultures also yielded *Streptococcus mitis* group. After completion of ceftriaxone, he was observed off of antibiotics for 2 months to ensure no recrudescence of infection. He then successfully underwent implantation of a rotating hinge TKA with long stem components. Intraoperatively, there was no sign of infection and intraoperative pathology and aerobic and anaerobic cultures were negative. He was then placed on a 3-month course of doxycycline as secondary prophylaxis.

**Clinical Pearls**

1. The diagnosis and management of PJI requires a multidisciplinary team to provide a successful outcome.
2. There is no gold standard for the diagnosis of PJI, and it requires collation by the clinician of the history, physical exam, and laboratory and radiology studies including synovial fluid and periprosthetic tissue examination and culture.
3. Medical management is dictated by the surgical management strategy.

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# Chapter 3
# *Cutibacterium acnes* and the Shoulder

**Michael P. Campbell and Alexander R. Vap**

## Book Chapter

A 37-year-old male with left shoulder pain for 9 months presents to the office for evaluation. He reports the pain as sharp and intermittent, and he rates it as a 5/10. He has pain with activities of daily living, specifically overhead movements. The pain awakens him at night. He also complains of crepitus and decreased range of motion.

He was previously seen by an outside orthopedic surgeon and underwent a shoulder arthroscopy, glenoid chondroplasty, partial synovectomy, and cartilage grafting with StimuBlast.

Additionally, he was recently seen by a rheumatologist for polyarthralgias. He was prescribed a course of steroids, which led to improvement in his symptoms. He underwent laboratory testing and was found to have a possible seronegative inflammatory arthritis. This was previously undiagnosed and he is undergoing further workup.

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J. Reznicek et al. (eds.), *Musculoskeletal Infections*,
https://doi.org/10.1007/978-3-030-41150-3_3

- PMH: None
- PSH: L knee ACL, PCL, MCL reconstruction
- Meds: Diclofenac, prednisone
- All: NKDA
- SH: Alcohol 1–2×/month. No tobacco. No illicit drug use. Retired from the Army
- FH: DM in father. No history of RA, lupus

## Physical Examination

- General: No acute distress, comfortable, well groomed
- Cardiovascular: Regular rate
- Pulmonary: Clear to auscultation bilaterally
- Abdomen: Soft, nontender, nondistended

### *Left Shoulder*

- Inspection: Well-healed incisions. No erythema or induration. No atrophy of supraspinatus, infraspinatus, deltoid, trapezius, or latissimus
- Palpation: Tender to palpation over anterior shoulder
- ROM: Limited passive range of motion, forward flexion 110 degrees, abduction 90 degrees, and external rotation 50 degrees. Limited active range of motion in all directions
- Rotator cuff: 5/5 supraspinatus, infraspinatus, teres minor, subscapularis
- Special tests: Negative Hawkins, negative Neer
- Neurologic: Motor: anterior interosseous nerve/posterior interosseous nerve/ulnar intact. Sensory: median/radial/ulnar intact

## Laboratory Findings

- WBC 6.2 Hgb 11.5 Hct 36.9 PLT 454
- BMP WNL
- Hepatic panel WNL

- Urinalysis neg
- CRP 5.6
- ESR 67
- RF < 15 (nl)
- ANA neg at 1:80
- Anti-CCP IgG neg

## Imaging

- Left shoulder x-ray (Figs. 3.1 and 3.2): Severe glenohumeral osteoarthritis with bone-on-bone articulation
- Left shoulder CT (Fig. 3.3): Severe degeneration of humeral head and glenoid
- Left shoulder MRI (Fig. 3.4): Advanced joint destruction with extensive erosive changes of humeral head and glenoid. Large effusion. Extensive synovitis

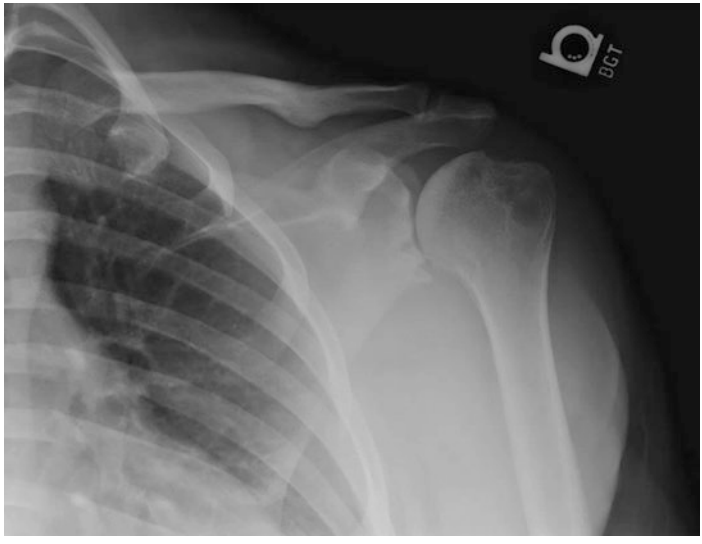


FIGURE 3.1 AP radiograph of shoulder demonstrating severe arthritis with bone-on-bone articulation

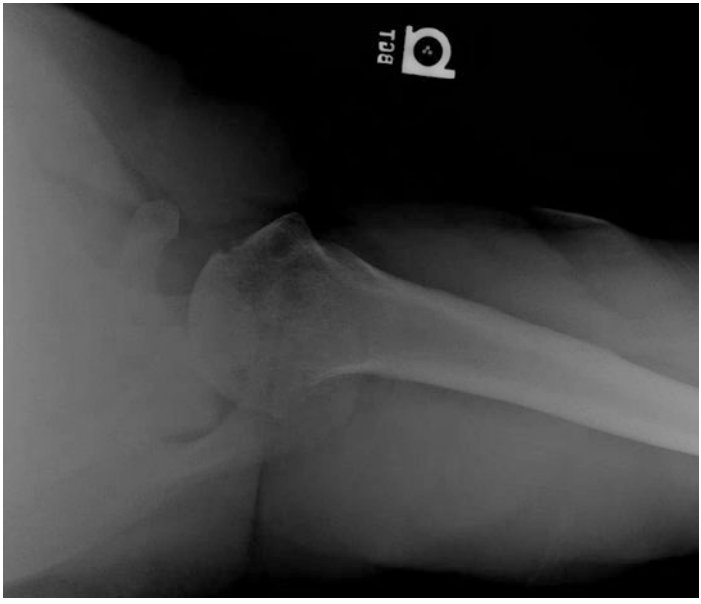


FIGURE 3.2 Axillary radiograph once again demonstrating severe arthritis

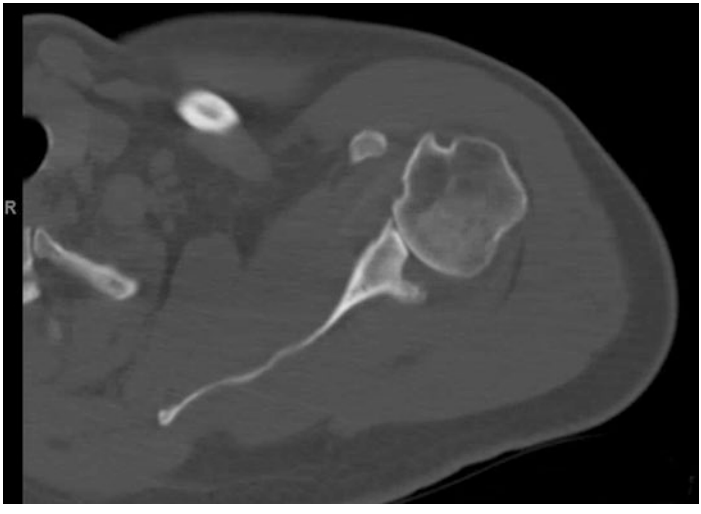


FIGURE 3.3 Axial CT scan showing degeneration of humeral head and glenoid

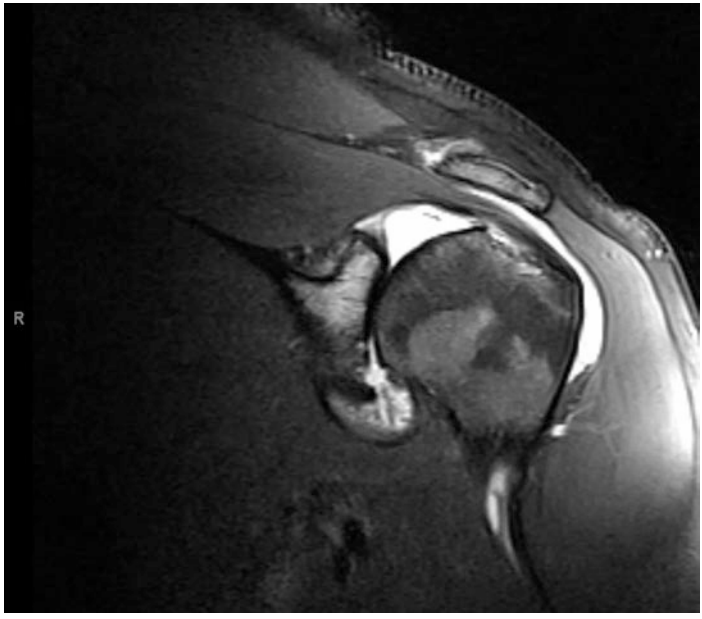


FIGURE 3.4 Coronal T2-weighted MR image demonstrating chondral damage with extensive synovitis and large effusion

**Question** What is your preliminary diagnosis?

**Preliminary Diagnosis** Left glenohumeral seronegative arthropathy

## *Medical Decision-Making*

After discussion of risks and benefits of surgery with the patient, the decision was made to undergo shoulder arthroscopy with synovial biopsy to rule out infection as a cause of his early-onset arthritis.

Left shoulder arthroscopy findings (Figs. 3.5 and 3.6):

1. Grade 4 arthritis of glenoid and humeral head
2. Fraying of the undersurface of supraspinatus, but supraspinatus, infraspinatus, subscapularis intact

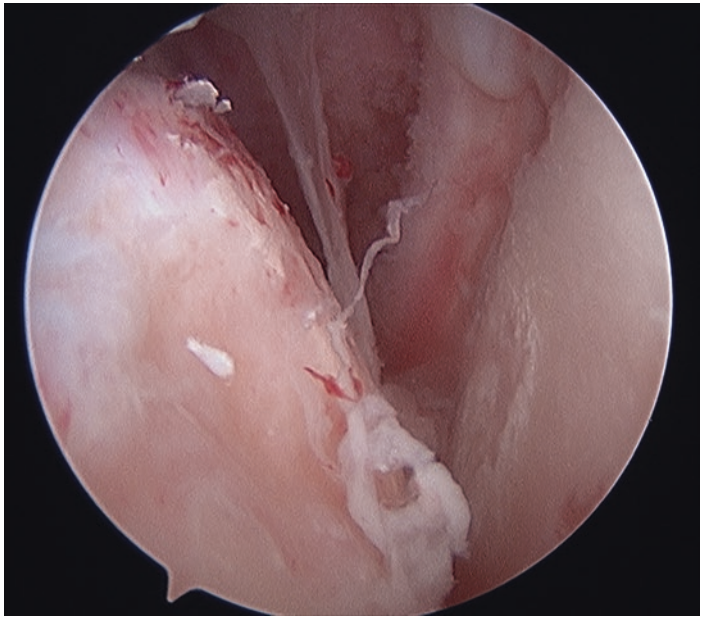

Figure 3.5 Arthroscopic image demonstrating grade 4 changes to humeral head and glenoid with labral fraying

3. Fraying of anterior and posterior labrum
4. Extensive synovitis

Aspirate: *Cutibacterium acnes* (sensitive to penicillin)

Tissue culture: *Cutibacterium acnes* (sensitive to penicillin)

At this time, the patient was referred to infectious disease specialist to be treated for his native glenohumeral septic arthritis, prior to total shoulder arthroplasty. He was treated with 2 grams IV ceftriaxone daily for 4 weeks followed by amoxicillin 500 mg po three times daily for 2 weeks. After discussing with the infectious disease specialist following antibiotic treatment, it was agreed upon to proceed with total shoulder arthroplasty (TSA).

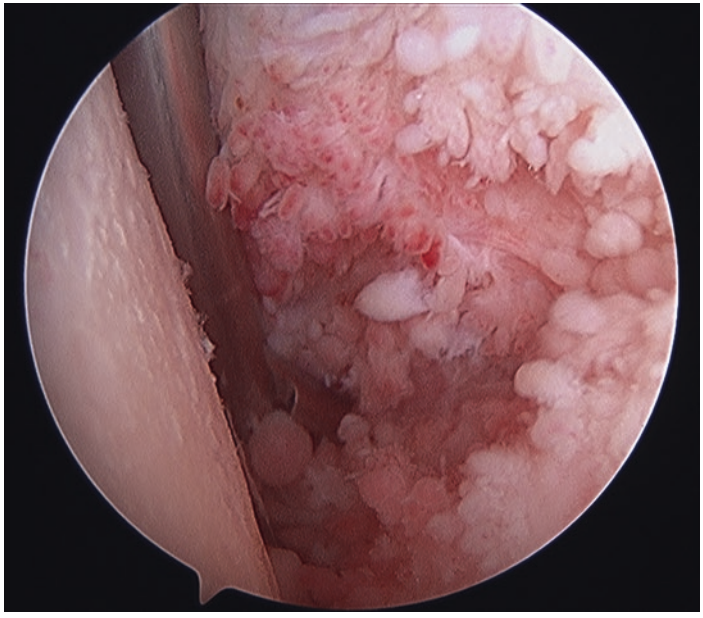

FIGURE 3.6 Arthroscopic image showing extensive synovitis within glenohumeral joint

The patient underwent an uncomplicated TSA with posterior augmented glenoid (Fig. 3.7), and he is rehabilitating well.

**Final Diagnosis** Left glenohumeral seronegative arthropathy complicated by native shoulder septic arthritis.

## Discussion

*Cutibacterium acnes* is a low virulent, indolent organism without typical signs and symptoms of infection. Delayed diagnosis following shoulder arthroplasty is well recognized, but native joint septic arthritis may be under-recognized and

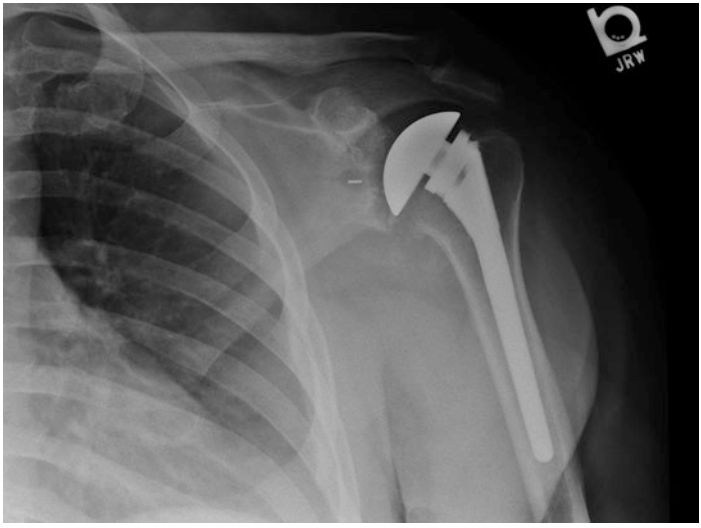


Figure 3.7 AP radiograph showing total shoulder arthroplasty with posterior augmented glenoid

undiagnosed [1].[1] Arthrocentesis and tissue culture should be considered for joints with chronic inflammatory arthritis prior to steroid injection or joint arthroplasty. The shoulder and axilla is heavily colonized with *Cutibacterium acnes* [2].[2] There is evidence of a low-abundance microbiome in the subdermal tissues of the shoulder, including the supraspinatus, and possibly other areas of the rotator cuff [3].[3]

The shoulder is the most frequent location of *C. acnes* prosthetic infection [4].[4] Diagnosis is difficult, because the patient will typically present with long-standing pain and stiffness, rather than local signs of infection such as warmth, or a draining sinus. Systemic symptoms, such as fever, are absent as well. Microbiological diagnosis is difficult and requires high-quality samples with cultures held for a prolonged period of time [4].[4]

[1] Native joint *Cutibacterium*

[2] *P. acnes* colonization

[3] *C. acnes* and the shoulder microbiome

[4] *C. acnes*: dx and tx

**Clinical Pearls**

1. Early-onset arthritis in the young patient population with history of surgical intervention and/or injection should raise your concern for alternate diagnoses including inflammatory arthropathy and septic arthritis.
2. *Cutibacterium acnes* can present as an indolent process. Typically it presents as long-standing pain.
3. Prior to joint replacement, it is important to rule out infection, especially in the setting of an elevated CRP and ESR. Synovial biopsy is the gold standard.

The findings of early-onset arthritis in the younger patient population (<40 years of age) with a history of surgical intervention and/or injection should raise concern for alternate diagnoses other than osteoarthritis, including inflammatory arthritis and septic arthritis.

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# Chapter 4
# Initial Open Fracture Management

**Yelena Bogdan**

## Case: Grade 3A Open Tibia Fracture

A 27-year-old healthy male sustained an isolated severe musculoskeletal injury to his right leg while working on a forklift (Fig. 4.1). After splint stabilization of the extremity, he had present sensation in his foot with dopplerable pulses and was able to move his toes. On further examination, he had a large near-circumferential wound (Fig. 4.2). He was immediately administered weight-based cefazolin and gentamicin for his open fracture and taken that night to the operating room for urgent debridement with external fixation of the ankle and fibula stabilization (Fig. 4.3). He subsequently underwent multiple staged surgeries including intramedullary nail fixation of the tibia with first-stage Masquelet (induced membrane) procedure and primary wound closure. He later underwent second-stage bone grafting with iliac crest autograft and subsequently healed with a stiff but functional ankle (Fig. 4.4).

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J. Reznicek et al. (eds.), *Musculoskeletal Infections*,
https://doi.org/10.1007/978-3-030-41150-3_4

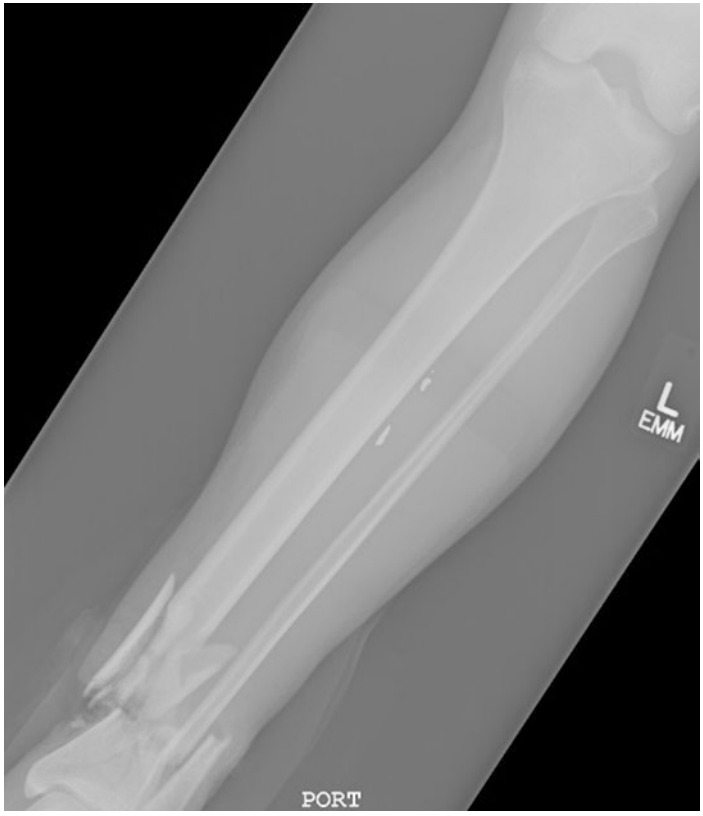


FIGURE 4.1 Initial X-rays of tibia and fibula showing a severe distal injury with bone loss

## Discussion

### *Classification*

Open fracture management begins with the classification of the injury, developed by Gustilo and Anderson, which is predictive of infection rates [1]. It is based on the size and severity of the traumatic open wound, as well as additional factors including need for soft tissue coverage, severe con-

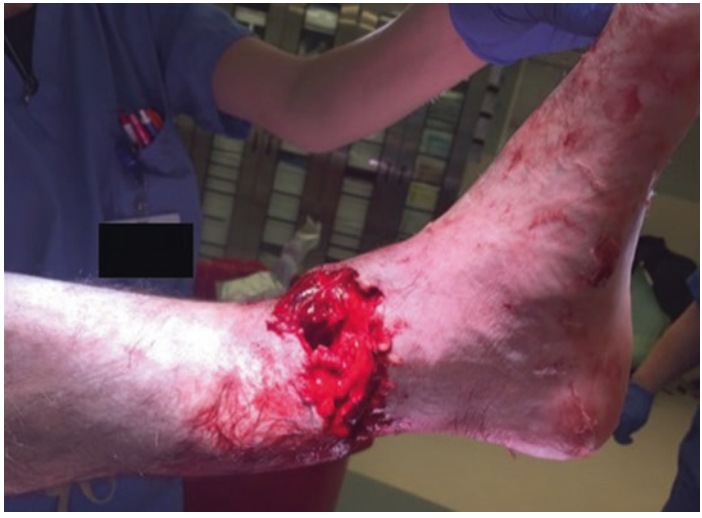

FIGURE 4.2 Clinical photo of medial wound

tamination, or vascular repair. Grade 1 is a relatively low-energy injury with a wound less than 1 cm in length. Grade 2 wounds are between 1 and 10 cm, have minimal comminution, no extensive contamination, and can be closed primarily. Grade 3 fractures include wounds greater than 10 cm, extensive soft tissue damage (such as shotgun injuries), and segmental fractures regardless of wound size. Grade 3 open injuries are further subdivided into three types: Grade 3A are injuries with adequate soft tissue coverage; Grade 3B require rotational or free flap coverage; and Grade 3C comprise any injury with a concomitant vascular injury requiring repair, regardless of bony or soft tissue severity [2]. Other classification systems, such as the one developed by the Orthopaedic Trauma Association [3], have good predictive ability in terms of treatment and amputation; however, these are not as popular or as widely used.

This patient had a large wound greater than 10 cm in size, and we were able to achieve primary wound closure without a need for flap coverage; therefore his fracture is graded as a 3A.

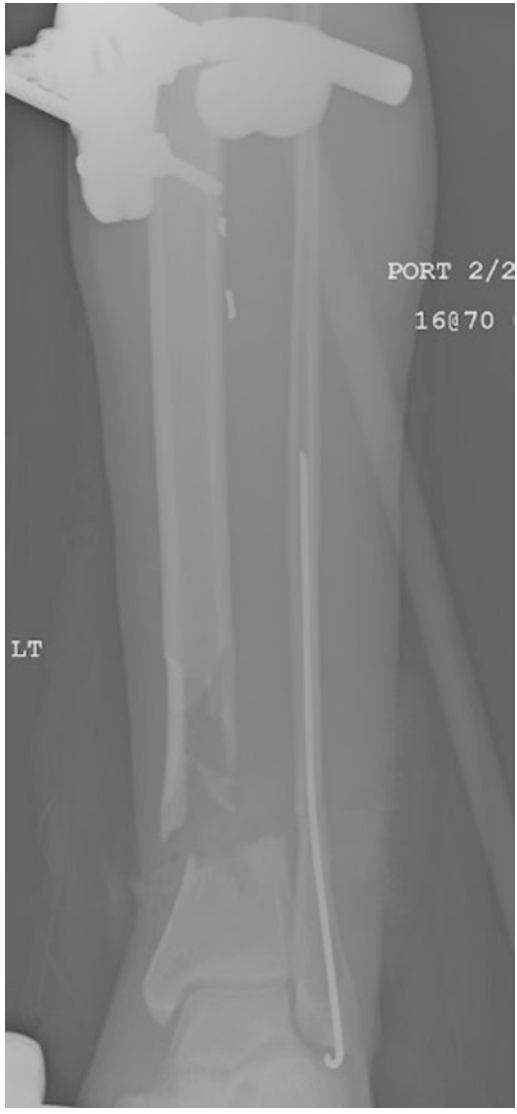


Figure 4.3 Provisional stabilization with external fixation and fixation of fibula

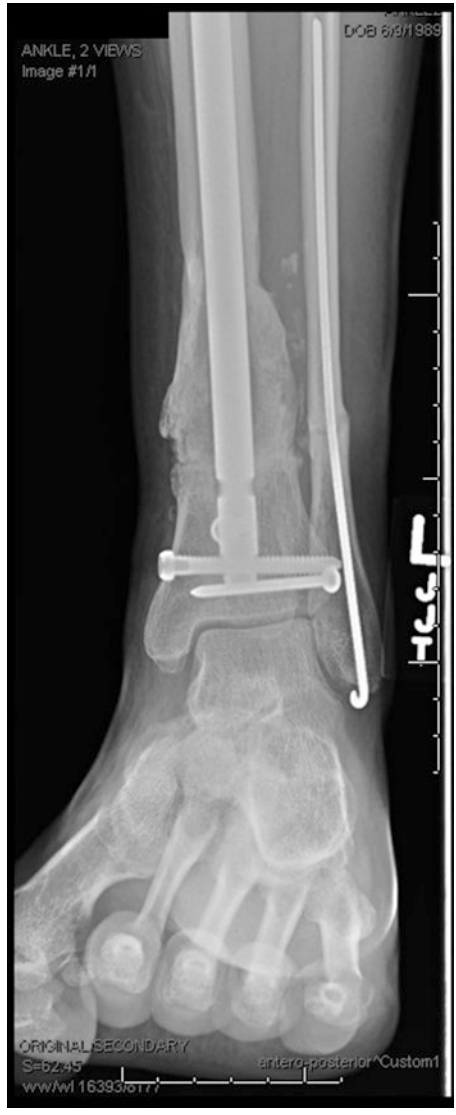


FIGURE 4.4 Final X-rays at 1 year, successful healing

## *Initial Management*

The mainstays of open fracture management include irrigation and debridement of the open wound, soft tissue management, antibiotic administration, and skeletal stabilization. Of these, the quality of debridement is vitally important, particularly for Grade 3 injuries. After a thorough initial assessment of the limb, including a diligent search for neurovascular compromise and/or the presence of compartment syndrome, irrigation and debridement of all devitalized tissue should be performed as soon as feasible [2]. The timing of debridement is controversial, with some studies showing that the historical "6-hour rule" has little support in the literature. A systematic review of 16 trials comprising more than 3000 open fractures showed no difference in infection rates, even with a cutoff of 12 hours to debridement [4]. If the wound cannot be closed primarily, repeat debridements are done at 48-hour intervals until closure or flap coverage. A negative pressure dressing in between debridements has been shown to decrease infection risk, compared to control mesh dressings, in one randomized trial [5]. Wound closure should be achieved as soon as possible, provided an adequate debridement is accomplished. Skeletal stabilization is dependent on patient physiology, status of the wound, and the judgment of the surgeon; the ideal scenario is early wound coverage combined with fracture stability to provide soft tissue support.

While the nuances of irrigation are less important than achieving an adequate debridement, certain protocols are more frequently practiced. The threshold adequate volume of irrigant is unknown, but most surgeons use the "3-6-9" rule, with 3 liters for Grade 1, 6 liters for Grade 2, and 9 liters for Grade 3 fractures [6]. The goal of irrigation is to remove, rather than kill, bacteria, and so the judgment of the surgeon is paramount to determine the proper extent to prevent the bacteria from propagating and forming biofilm. The contents of the solution were examined in several trials. Anglen's randomized study showed no difference in infection rates between soap and bacitracin solutions in 400 patients [7].

More recently, the large multicenter randomized FLOW trial of 2447 open fractures showed higher rates of reoperation in the soap irrigant group than the normal saline group [8]. Thus, normal saline is recommended. Irrigation pressure was also examined in that trial, with no difference between high- and low-pressure lavage. Additionally, an earlier trial showed high-pressure lavage to cause deeper bacterial penetration into wounds, and so it is not recommended unless severe contamination requires it [9]. Initial cultures of the wound are not useful due to the low yield of organism isolation. A 2000 study showed initial cultures to be positive only 35% of the time, and in infected wounds the organism matched initial cultures only 18% of the time [10]. Post-debridement cultures are useful in cases of unusual environmental contamination, such as marine organisms [2].

In this patient, expedient irrigation and debridement was performed in the operating room with 9 liters of normal saline under low pressure, and the fracture was temporarily stabilized with external fixation, with immediate fixation of the fibula using a minimally invasive technique. This helped achieve initial stability until he could undergo definitive fixation, which occurred during the "second-look" debridement. The wound bed was clean at that time, and no cultures were taken.

## Antibiotics

Antibiotic administration is essential to the acute management of open fractures [11]. Compared with placebo, antibiotics decrease the rate of infection by a factor of 6 [12]. The choice of drug, timing of administration, and duration of therapy are controversial. The most frequently used combination is a first-generation cephalosporin (usually cefazolin) and an aminoglycoside (gentamicin), to cover both gram-positive and gram-negative pathogens. Fluoroquinolones can also be used as a substitute for gram-negative coverage. Penicillin is added for Grade 3 fractures with soil contamination, farm injuries, or environments favoring anaerobic proliferation [2].

This combination therapy has been shown to decrease infection, with a 4.6% rate versus 13% with cephalosporin alone [13]; however, Grade 1 and 2 fractures were not separated in that study. Other authors suggest only cephalosporin in Grade 1 and 2 fractures and adding an aminoglycoside in Grade 3 [14]. This is supported by more recent studies, which show that a protocol using only cefazolin for Grade 1 and 2 fractures did not increase infection rates [15]. With the rise of MRSA (methicillin-resistant *Staph. aureus*) infections, some surgeons have added vancomycin to their regimen [16]; however, at least one randomized trial showed no difference in MRSA infections with the addition of vancomycin [17].

The timing of administration is crucial to preventing infection before bacteria forms biofilm, which antibiotics cannot penetrate well. Both animal [18] and human clinical [19] studies show that the earlier the antibiotic is administered, the better chance of preventing infection. Delay of antibiotic administration has a detrimental effect on infection rates, even if time to debridement is decreased [18]. One study showed a delay of greater than 5 days to wound coverage and antibiotic administration greater than 66 minutes to be independent predictors of infection [19]; therefore, antibiotic administration within an hour of injury is ideal. This practice has been widely adopted by orthopedic traumatologists [20].

The optimal duration of antibiotic therapy is not known, with some surgeons continuing until wound coverage is achieved [1] and others stopping after a short course [21]. A review of randomized controlled trials has found similar infection rates in courses of 1, 3, and 5 days after injury [11]. Currently, no evidence showing effectiveness beyond 24 hours exists, and surgeons are encouraged to limit antibiotic use and practice stewardship given bacterial resistance.

In this patient's case, the presence of a Grade 3 fracture warranted both a cephalosporin and aminoglycoside, which was administered upon arrival and stopped after 24 hours. He went on to heal without infection.

**Clinical Pearls**

1. Even fractures with small wounds can be high-grade, provided a high-energy mechanism exists.
2. As soon as clinically feasible, a thorough debridement of all devitalized tissue with irrigation via low-pressure normal saline is performed.
3. The optimal time for antibiotic administration is within an hour of injury.
4. Cephalosporin for 24 hours is used for Grade 1 and 2 fractures, with an aminoglycoside or fluoroquinolone added for Grade 3 fractures.
5. Wound closure and skeletal stabilization should be achieved as early as is safe, with wound coverage within 5 days.

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# Chapter 5
# Local Antibiotic Treatment for Open Fracture

**Gele B. Moloney**

## Case

A 55-year-old otherwise healthy male sustained a crush injury to the right leg resulting in a Gustilo and Anderson Type 3B (soft tissue loss requiring flap coverage) open tibia fracture (Fig. 5.1). Secondary survey found this to be an isolated injury. On physical examination the patient had an extensive wound overlying the anteromedial distal tibia. He was able to fire his extensor hallucis longus and flexor hallucis longus tendons and had preserved sensation in the superficial peroneal, deep peroneal, and tibial nerve distributions. Sensation was absent in the saphenous distribution. Pulses were diminished. CT angiogram of the extremity demonstrated disruption of the peroneal artery at the level of the fracture and stenosis of the anterior tibial artery which was entrapped between fracture fragments. The posterior tibial artery was preserved.

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J. Reznicek et al. (eds.), *Musculoskeletal Infections*,
https://doi.org/10.1007/978-3-030-41150-3_5

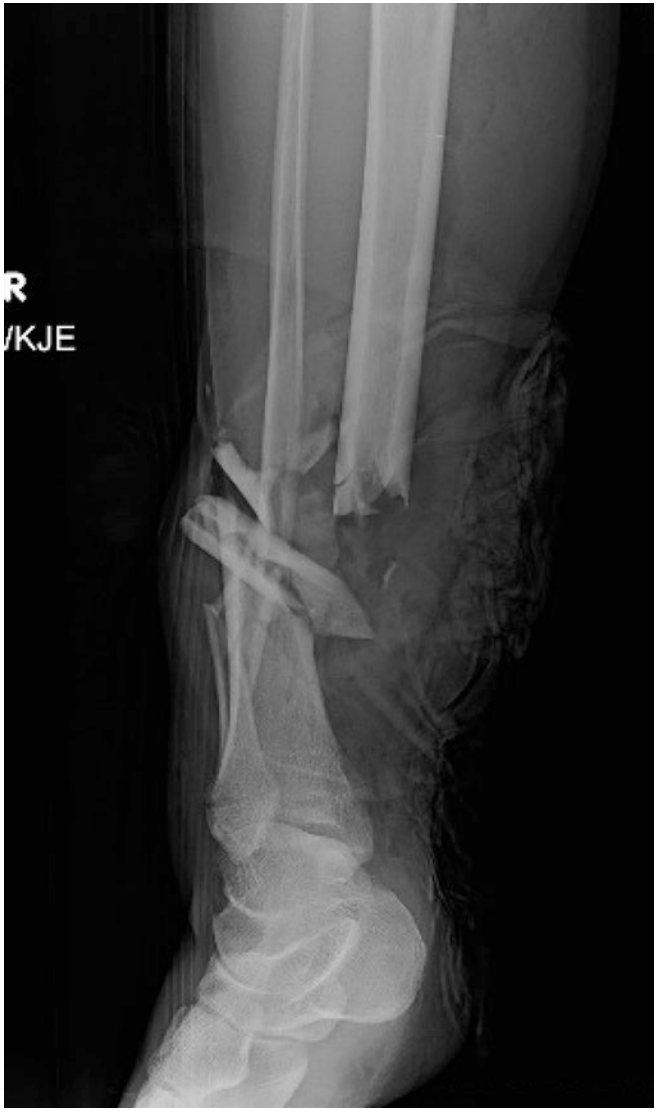


FIGURE 5.1 Radiograph of the right leg demonstrating a comminuted fracture of the distal tibia and fibula

Upon arrival in the emergency department, he was given tetanus vaccine and piperacillin-tazobactam for treatment of a Type 3 open fracture. He was taken urgently to the operating room where he underwent irrigation and debridement of his open fracture. Bone loss from his injury and debridement of nonviable bone resulted in a bone defect in the distal third of the tibia measuring 5 cm in length and 100% the circumference of the tibia. Antibiotic-impregnated polymethyl methacrylate (PMMA) beads were placed into the bone defect, and the patient was placed in an external fixator for temporary stabilization of his fracture. Extensive conversation was had with the patient regarding the limb-threatening nature of his injury, and he elected to proceed with attempted limb salvage.

He was subsequently taken back to the operating room where he underwent intramedullary nailing of his fracture, placement of a new antibiotic-impregnated PMMA spacer (Fig. 5.2), and placement of a rectus abdominis free flap to provide soft tissue coverage.

At 4 months postoperatively when his soft tissues were amenable to reoperation, he was taken back to the operating room where he underwent removal of the antibiotic spacer with bone grafting of his defect using reamer-irrigator-aspirator (RIA) autograft from the ipsilateral femur. At 1 year post injury, the soft tissue and fracture have healed without evidence of infection (Fig. 5.3a, b).

## Discussion

Open fracture of the tibia with bone and soft tissue loss is a limb-threatening injury which requires a coordinated multisystem approach to achieve limb salvage. Aggressive debridement in the operating room in a timely fashion is important in decreasing the likelihood of infection. The combination of traumatic bone loss and bone loss secondary to debridement can result in critical-sized bone defects which are unable to heal primarily. Additionally, trauma to the soft tissue envelope can diminish local blood flow and increase rates of infection.

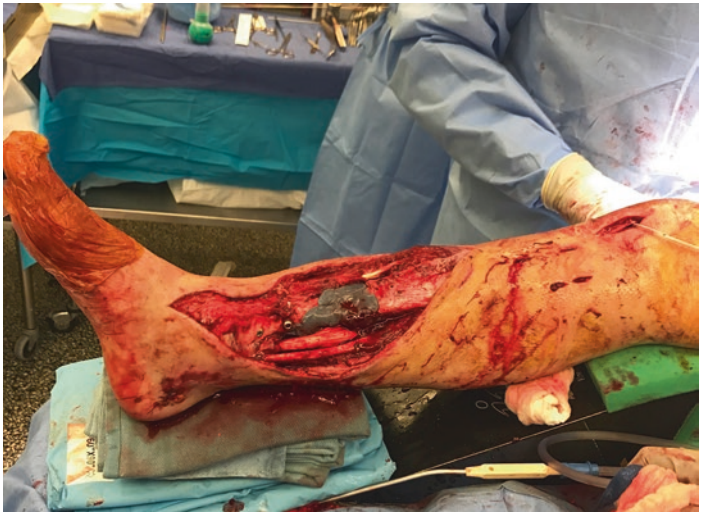

FIGURE 5.2 Intraoperative image of the right leg at the time of definitive intramedullary nail fixation, placement of antibiotic spacer, and flap coverage. Note the antibiotic spacer along the tibia in the center of the image and the significant soft tissue injury along the anteromedial leg

Insertion of an antibiotic-laden PMMA spacer into the bone defect serves multiple functions. First, local elution of antibiotics helps to sterilize a contaminated wound bed. Second, the spacer will fill the dead space left following debridement decreasing risk of hematoma formation, which can increase chance of infection. Additionally, as described by Masquelet [1], PMMA, even in the absence of antibiotics, will result in formation of a biologically active membrane, which serves as an excellent foundation for staged bone grafting.

There are several combinations of antibiotics which can be used in this setting. While the optimal combination and dosing has not been fully elucidated, the most commonly used antibiotic combination includes vancomycin with tobramycin

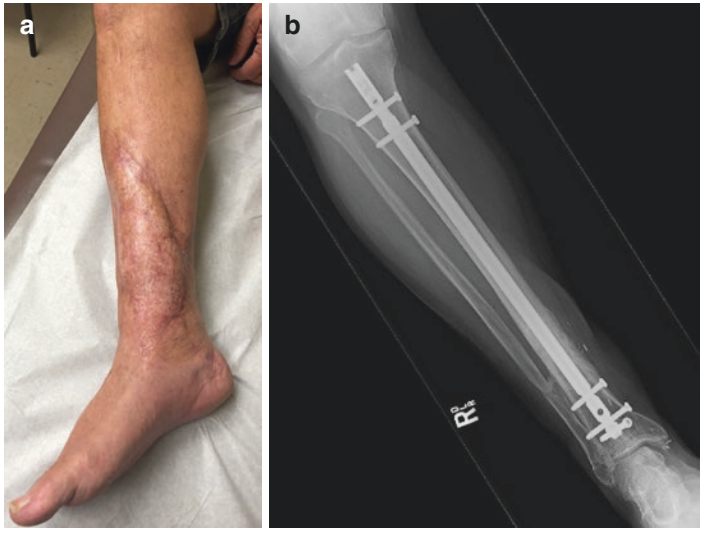


FIGURE 5.3 (**a**) Clinical photograph of the right leg at 1 year demonstrating a healed free flap covering the prior traumatic soft tissue wound. (**b**) Radiograph of the right leg at 1 year demonstrating healed distal tibia and fibula fractures

or gentamicin, as infections following open fractures result from a combination of gram-positive and gram-negative organisms [2]. Certain companies offer PMMA which comes premixed with antibiotics or the antibiotics can be added at the time of cement mixing. The data on peak levels and timing of local elution of antibiotics varies but confirms sufficient local levels to inhibit bacterial growth [3].

The care of the open fracture with bone loss is complex and requires multidisciplinary care. Local antibiotics delivered utilizing PMMA cement can play a role in the management of these challenging fractures but must be utilized in addition to meticulous surgical debridement and systemic antibiotics.

**Clinical Pearls**

1. Local antibiotics can be utilized in the care of open fractures to help decrease bacterial contamination but are not a substitute for adequate operative debridement.
2. Antibiotic-impregnated PMMA can be utilized during the first stage of induced membrane (Masquelet) technique to treat segmental bone defects associated with open fracture.
3. The use of local antibiotics is part of a complex treatment plan but does not replace the need for systemic parenteral antibiotics for open fracture.

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# Chapter 6
# Infected Nonunion of the Tibia

**Naomi E. Gadinsky, Ashley E. Levack, and David S. Wellman**

## Abbreviations

| | |
|---|---|
| I&D | Irrigation and debridement |
| PMMA | Polymethylmethacrylate |
| RIA | Reamer-irrigator-aspirator |

## Case

A 48-year-old male was in a motor vehicle accident and sustained an open fracture of the distal third of the right tibia and fibula. He initially presented to an outside institution where the fracture was debrided and stabilized with an external fixator, followed by open reduction and internal fixation. The patient developed an open wound on the medial aspect of the right leg and an underlying bony infection was evident. He underwent removal of hardware, which was complicated by

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J. Reznicek et al. (eds.), *Musculoskeletal Infections*,
https://doi.org/10.1007/978-3-030-41150-3_6

intraoperative breakage of two screws that were left embedded in the tibia. This was followed by multiple procedures including irrigation and debridement (I&D) of the infected areas, placement of antibiotic beads around the fracture site, and wound coverage with a fasciocutaneous free flap from the right anterolateral thigh. The patient then underwent revision internal fixation including bone graft approximately 5 months from the initial injury. Unfortunately, he developed another infection and wound complications requiring multiple I&Ds, hardware removal, and further local wound coverage with fasciocutaneous advancement flaps at 12 months from injury (7 months from the revision internal fixation with bone grafting). At this point, the patient had undergone 16 surgeries to the right leg and had been treated with multiple rounds of antibiotics for polymicrobial osteomyelitis.

The patient first presented to our institution for further management of his chronic infected nonunion 15 months from injury (Fig. 6.1). The surgical plan involved a multistage revision. The first stage of this reconstruction included aggressive debridement and resection of infected bone and placement of an antibiotic-loaded bone cement spacer into the osseous defect in the style of Masquelet. Once the overt infection had been treated, a new free flap provided soft tissue coverage of the open wound, as the previous soft tissue coverage procedures were unsuccessful in providing an adequate soft tissue envelope. Finally, a completion of the Masquelet procedure (in which the antibiotic-impregnated cement spacer is removed and the bone void filled with bone autograft) was performed along with definitive fixation of the bone with internal hardware. Two surgeons were involved in the patient's care, including an orthopedic trauma fellowship-trained surgeon and an orthopedic hand surgeon with additional plastic surgery fellowship training and expertise in soft tissue management and free flaps.

During the first stage of the revision, a thorough I&D was performed with complete removal of the retained broken screws in the tibia, resection of infected bone, antibiotic cement spacer block placement, antibiotic intramedullary nail placement, and application of an external

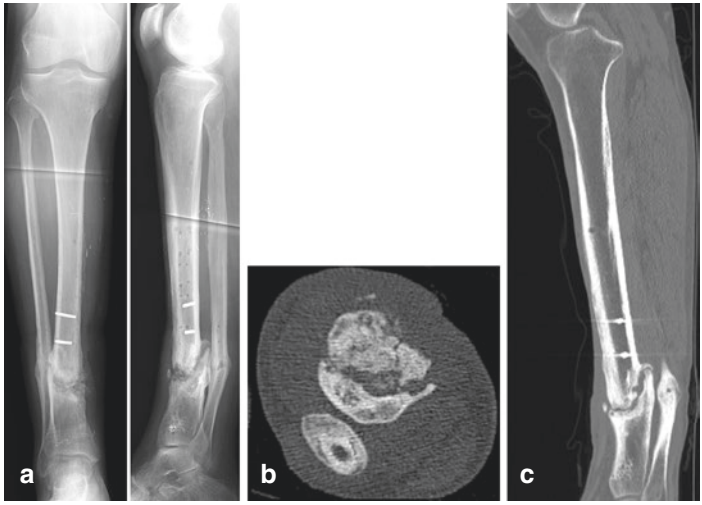


FIGURE 6.1 Radiographs and CT images from the patient's initial presentation to our institution reveal the presence of an unhealed right distal tibial nonunion with broken screw pieces embedded in the tibia. (**a**) AP and lateral radiographs of the right tibia. (**b**) Axial CT image of the right tibia. (**c**) Sagittal CT image of the right tibia

fixator (Fig. 6.2). Cultures showed infection with methicillin-susceptible *Staphylococcus aureus*. The patient then underwent multiple additional I&D procedures and eventual wound coverage with a gracilis free flap and split-thickness skin graft from the right thigh. At 17 months from injury, the patient underwent a final definitive fixation procedure with removal of the antibiotic nail, removal of the Masquelet cement block, filling of the osseous defect with bone graft harvested in a retrograde fashion from the right femur using a reamer-irrigator-aspirator (RIA), and insertion of a definitive intramedullary nail (Fig. 6.3). While under our care, the patient was seen regularly by an infectious disease specialist for management of his systemic antibiotic regimen.

Progressive healing was noted at routine follow-up appointments, and complete osseous union was noted at 29 months from the initial injury. Bone cultures from the final surgery

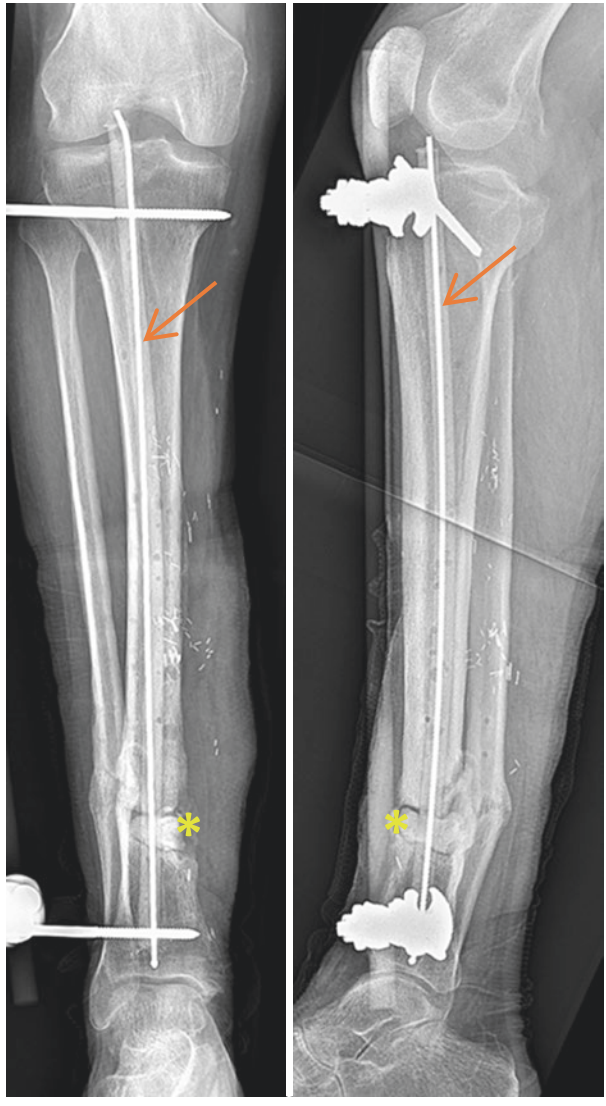

FIGURE 6.2 AP and lateral radiographs of the right tibia after the first stage of our revision reveal a bone graft spacer filling the osseous defect, an antibiotic intramedullary rod, and an external fixator in place. Arrow: Antibiotic-impregnated cement surrounding intramedullary guidewire. Asterisk: Antibiotic-impregnated cement spacer filling bone void

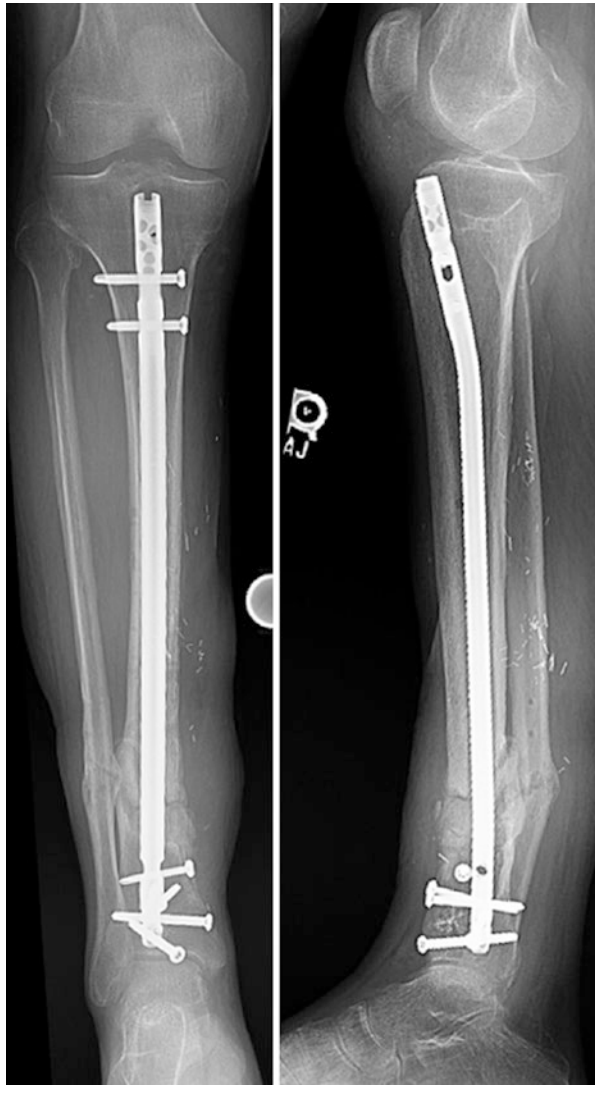

FIGURE 6.3 AP and lateral radiographs of the right tibia after the second stage of our revision reveal interval removal of the external fixator, a bone graft filling the osseous void, and definitive fixation with an intramedullary nail

showed no growth, indicating eradication of the infection at the fracture site. Due to irritation from the hardware, the patient underwent uneventful removal of the intramedullary nail and all interlocking screws at 4 years from the initial injury. At the latest follow-up appointment, the patient exhibited full use of his right leg with intact motor and sensory function, full knee range of motion from 0° to 140°, well-healed incisions, and a viable skin flap. Final radiographs revealed a fully healed tibia (Fig. 6.4). To achieve this outcome, the patient had undergone over 20 surgeries over the course of 4 years.

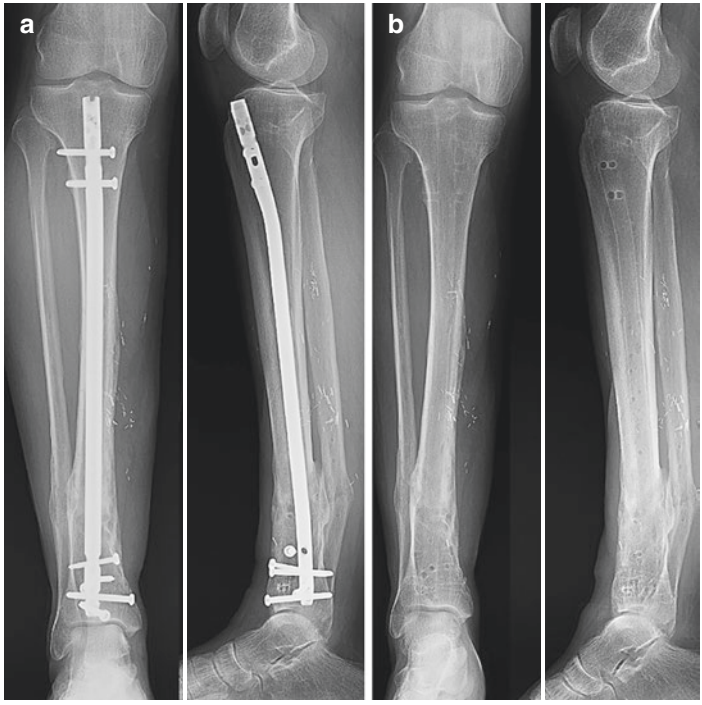


Figure 6.4 (**a**) AP and lateral radiographs at the final follow-up before hardware removal showing a healed distal tibia-fibula fracture with intact hardware. (**b**) AP and lateral radiographs at the latest follow-up after hardware removal showing a healed tibia with no hardware in place

## Discussion

### *Open Tibia Fractures*

Tibia-fibula fractures have the among the highest nonunion rates of all long bones, with rates up to 14% [1]. Open tibia fractures have particularly high rates of nonunion and delayed union, and rates of revision surgery for slow healing have been reported between 12% and 41.1% [2, 3]. Nonunions are often due to infection, with infection rates following open tibia fractures ranging from 10% to 30% depending on injury severity [2–4]. These high nonunion and infection rates can be explained by the high-energy injury mechanisms and significant soft tissue disruption often associated with open tibia fractures [3].

As shown by the above case example, these injuries can have devastating effects on patients' lives. Multiple procedures, long courses of antibiotics, numerous costly hospital admissions, and the potential for amputation have significant effects on quality of life. At 12 months post-injury, many patients with tibial shaft fractures still exhibit diminished quality of life measures compared to baseline, with open injuries showing significantly lower Short-Form Six-Dimension (SF-6D) scores compared to closed injuries [5]. Because of these serious complications, prevention of progression to an infected nonunion is paramount.

Initial open fracture management includes emergent administration of intravenous antibiotics as well as local I&D of the injury site. While I&D within 6 hours of injury has been thought of as a general rule [6, 7], the timing of I&D remains debated in trauma literature. Namdari et al. showed that 42% of patients with open tibia fractures received I&D greater than 6 hours from injury and that this delay was associated with age, head or thoracic injury, higher injury score, presentation late at night, and type of hospital setting [7]. There has not been substantial literature supporting decreased infection rates for open fractures debrided within 6 hours, and many surgeons feel comfortable debriding lower-grade open tibia

fractures the next morning [6]. Higher-grade, highly contaminated open fractures represent greater infection risk and therefore should be debrided more promptly.

## *Risk Factors for Infected Nonunion*

Despite proper initial management of open fractures, these complicated injury types still may progress to infected nonunions with chronic posttraumatic osteomyelitis. Open tibia fractures are contaminated by bacteria from the surrounding environment at the time of injury. High-energy injury mechanisms cause soft tissue devitalization and potential vascular disruption, further contributing to the risk of persistent infection and poor bony healing following these injuries. Undergoing multiple surgical procedures and long hospital stays also provide opportunities for contamination. Comorbidities such as diabetes and smoking further increase infection risk [8].

Certain bacteria form biofilms on implant surfaces and devitalized bone, making infected nonunions difficult to treat [4]. *Staphylococcus aureus* is the most commonly isolated bacteria from infected nonunions and is present in combination with other organisms in 65–70% of patients [4, 9]. Osteomyelitis is typically polymicrobial, with multiple organisms reported in 32–70% of patients [4, 9].

## *Diagnosis of Infected Nonunion*

Patients with an infected nonunion may present in different ways. Tenderness over the fracture site and painful ambulation raise concern for the presence of an unhealed tibia fracture. Some patients may present with overt signs of infection, including erythema, open wounds, or sinus tracts with purulent drainage [4]. Other patients without overt skin and soft tissue involvement may present with a persistently nonhealing fracture or a refracture of a seemingly healed bone.

Mills et al. found occult infection in 5% of patients thought to have aseptic nonunions [10], while Amorosa et al. reported positive intraoperative cultures in 28.7% of patients with presumed aseptic diaphyseal nonunions [11]. Therefore, a high index of suspicion is necessary even in patients without obvious signs of infection.

Infection should always be suspected. The workup for an infected nonunion and chronic osteomyelitis involves laboratory testing, imaging, and culture data. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels may be elevated as markers of inflammation. White blood cell (WBC) count may be elevated in patients with active soft tissue or wound infections, but generally is not elevated by the infected nonunion itself.

Plain radiographs are useful for evaluating fracture healing, persistence of fracture lucencies, and hardware complications that may indicate persistent motion at the fracture site such as implant breakage or screw migration. Additionally, overall limb alignment is typically assessed with long-leg standing plain films. Computed tomography (CT) scans are then obtained to better characterize the extent of any bridging callus, confirm the absence of fracture union, and assist with future surgical planning. One critical benefit of the CT scan is the ability to look for sequestered fragments and overt signs of osteonecrosis. These areas must be removed as they represent safe harbors for bacteria. Magnetic resonance imaging (MRI) is especially sensitive for evaluating patients for the presence of osteomyelitis, but does not typically aid in the diagnosis of nonunion [4].

Culture results with pathogen identification are the best way to confirm diagnosis of an infected nonunion. Intraoperative cultures should be taken during surgical debridement from bone, soft tissue, wound beds, sinus tracts, and purulent drainage if present. It is important to be aware of any antibiotics given prior to obtaining cultures, as this may affect results. Our protocol includes taking at least five cultures to help rule out contaminants and identify polymicrobial species.

## *Treatment of Infected Nonunion*

### Eradication of Infection

When presented with a chronically infected nonunion, all attempts must be made to eradicate the infection or the fracture site will not heal. This is the first and most critical step in treatment. Intravenous (IV) and/or oral antibiotics should be administered and managed by an infectious disease specialist based on culture sensitivities. Surgically, removal of infected hardware and/or foreign bodies (such as the broken screw bits in our case example) and aggressive serial debridement of infected and necrotic bone should be performed. Following hardware removal and bone resection, rigid external fixation is often used for provisional fracture stabilization during this stage of treatment, as this allows bony stability without placing hardware in the zone of infection.

Antibiotics may also be placed locally at the nonunion site to help treat the infection. Antibiotic-impregnated bone cement, or polymethylmethacrylate (PMMA), is the gold standard for local antibiotic delivery. Antibiotic-laden PMMA can be fashioned as beads, larger block spacers, or antibiotic-PMMA coated intramedullary implants [12]. Multiple authors report success treating infected tibial nonunions with antibiotic cement-coated interlocking intramedullary nails using gentamicin or tobramycin/vancomycin [9, 12]. These constructs simultaneously stabilize the fracture site while treating the infection and in certain patients can potentially treat infected nonunions in a single operation, saving them from a two-stage revision procedure.

Alternatively, an induced membrane (Masquelet) technique is a two-stage procedure that has gained popularity for treating infected nonunions with large bone gaps [8, 13–15]. In this technique, antibiotic-impregnated PMMA spacers are inserted into the bony defect at the time of final I&D. This serves to locally treat the infection as well as to induce the development of a highly vascularized membrane

containing growth factors around the cement spacer. After approximately 4–6 weeks, the spacer is removed, leaving the vascularized membrane intact, and the void is filled with bone graft. The fracture is stabilized with internal hardware. This sequence of procedures helps clear the infection and promote bony healing across large gaps that could not otherwise fill on their own.

## Addressing Soft Tissue Defects

During the initial management of the infection, soft tissue defects should be addressed. When necessary, flap coverage (free, rotational, or local advancement) and skin grafts can be used to provide wound coverage. These techniques should be performed by a surgeon with advanced training in free flaps and soft tissue coverage, such as a plastic surgeon, in order to maximize results. Soft issue coverage helps in eradicating the infection, as healthy tissue prevents new bacterial contamination and serves as a delivery system for IV antibiotics into a previously deficient area.

Free flaps are particularly useful in distal tibia fractures, tibia fractures with large soft tissue defects, and fractures with wound complications requiring revision procedures. Nieminen et al. evaluated a series of tibia fractures treated with internal fixation that developed complications leading to bone or hardware exposure requiring free flap coverage. They reported 13/15 (86.6%) of patients achieved successful flap healing with intact skin and no infections at final follow-up [16]. Muscle flaps also have been successful in treating wounds and sinus tracts caused by chronic osteomyelitis, with one study reporting a 91% success rate in patients with localized lower extremity osteomyelitis [17]. Soft tissue coverage should be achieved before definitive fixation in order to provide coverage of any new hardware that is inserted and should be considered a crucial part of the infection treatment portion of care.

## Addressing Osseous Defects and Definitive Fracture Fixation

Once the infection is under control and soft tissue defects have been addressed, definitive fixation of the fracture nonunion site with treatment of bony defects can be attempted. Many types of bone graft exist, including autograft, allograft, vascularized free fibula transfer, and Ilizarov-style bone transport. As discussed previously, the Masquelet technique is a two-stage procedure used for treating infected nonunions and tibia fractures with large bone defects, with success rates reported between 85% and 100% [8, 13–15]. In our case's first stage, an antibiotic-impregnated spacer was used to fill the bone defect, and an external fixator was applied, with replacement with bone autograft and definitive fixation performed in the second stage. Liu et al. evaluated 16 patients with infected gap nonunions treated with this technique and reported a 100% healing rate with an average healing time of 7.4 months [13]. Mühlhäusser et al. looked at a small series of patients with infected open tibia fractures treated with the Masquelet technique and saw clinical and radiographic healing in 7/8 patients (87.5%) [14].

To obtain bone graft for the second stage of the procedure, iliac crest bone graft and autograft from the femur via the reamer-irrigator-aspirator (RIA) technique are both viable options. Although iliac crest bone graft is viewed as the gold standard, RIA has shown similar union rates with improved postoperative pain, shorter harvesting times, and graft volume between 25 and 50 mL [18, 19]. In our case example, RIA harvest from the femur was performed during the same exposure used for tibial intramedullary nail placement, obviating the need for a separate iliac incision. In addition to filling bone voids, definitive fixation using intramedullary nails or plates and screws should be performed in accordance with standard principles of fracture fixation.

Although not used in our case example, the Ilizarov and "bone transport" technique can also be used to treat infected tibial nonunions with large bone gaps. This method utilizes dis-

traction osteogenesis via a specialized external fixator (Ilizarov apparatus) throughout the course of treatment. This allows the patient to fill in bone gaps through natural bone healing often without internal fixation. Similar to the Masquelet technique, success rates with Ilizarov protocols have been reported between 86.1% and 97.3% [20, 21]. However, patients are at risk of pin tract infection and must comply with wearing a cumbersome external fixator for many months.

## Patient Follow-Up and Counseling

Patients should be followed closely and monitored for the development of wound complications, recurrent infections, or hardware failure throughout the course of treatment. All physicians involved in the patient's care, including orthopedic surgeons, plastic surgeons, and infectious disease specialists, should follow the patient closely. Physical therapy should be utilized to help restore range of motion and function to the affected limb. As illustrated by the case example, eradication of infection, osseous union, and limb salvage with recovery of a functional limb can be achieved with time and a carefully executed treatment strategy. As demonstrated here, patients with open fractures that progress to infected nonunions must be counseled appropriately about the long recovery times, multiple surgical procedures, need for antibiotics, potential for amputation or loss of function, and the importance of close follow-up with all treating physicians.

**Clinical Pearls**

1. *Prevention of infected nonunions.* Open fractures that progress to infected nonunions are challenging to manage and devastating to patients. Treat all open fractures urgently with:
   - IV antibiotics
   - Irrigation and debridement

2. *Structured surgical approach*. Open fractures that progress to infected nonunions of the tibia should be treated with careful multistage surgical planning involving:
   - Infection control with debridement, resection, and both systemic and local antibiotics
   - Provisional external fixation when appropriate
   - Soft tissue coverage
   - Addressing bone defects
   - Definitive fixation of the fracture nonunion
3. *Multidisciplinary team approach*. Open fractures that progress to infected nonunions should be treated from a multidisciplinary team approach involving:
   - Orthopedic trauma surgeons
   - Plastic surgeons
   - Infectious disease specialists
   - Physical therapists

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# Chapter 7
# Infected Nonunion of the Clavicle

**James Shaw, Burak Altintas, Andy O. Miller, and David L. Helfet**

## Case: Infected Nonunion of an Open Clavicle Fracture

A healthy 45-year-old female sustained a grade I open left clavicle fracture after a fall from a horse. She was taken urgently to the operating room by the initial treating surgeon for single-stage irrigation and debridement of the open fracture followed by open reduction and internal fixation of the clavicle (Fig. 7.1a).

Four months later she continued to have pain and was found to have loosening of the clavicle fixation with absence of union at the fracture site (Fig. 7.1b). She was taken back to the operating room by the same surgeon for revision open reduction and internal fixation with repair of the nonunion with iliac crest bone grafting 5 months after her initial injury (Fig. 7.1c; top image).

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© Springer Nature Switzerland AG 2020

J. Reznicek et al. (eds.), *Musculoskeletal Infections*,
https://doi.org/10.1007/978-3-030-41150-3_7

Six weeks after the revision procedure, she continued to have pain, increased soft tissue swelling, and focal erythema around the middle of her incision. She returned to her surgeon and radiographs showed evidence of fixation failure and screw loosening (Fig. 7.1c; bottom image). She was given an oral course of cephalexin for 10 days, and her swelling and erythema resolved.

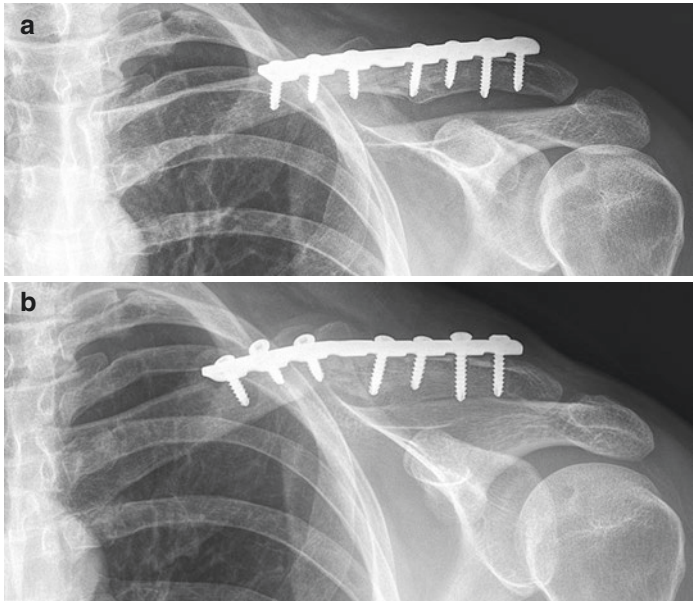


Figure 7.1 (**a**) Left clavicle radiograph after initial debridement of open fracture and primary fixation. (**b**) Left clavicle radiograph 4 months after index procedure demonstrating loosening of fixation and absence of union at fracture site. (**c**) Left clavicle radiograph after revision open reduction and bone grafting 5 months after index procedure. (bottom) Left clavicle radiograph 6 weeks after revision procedure demonstrating loosening of lateral screws. (**d**) Left clavicle intraoperative imaging after second revision procedure including hardware removal, soft tissue/osseous debridement, and dual plate fixation. (**e**) Left clavicle radiographs approximately 6 months after final procedure demonstrating healed fracture

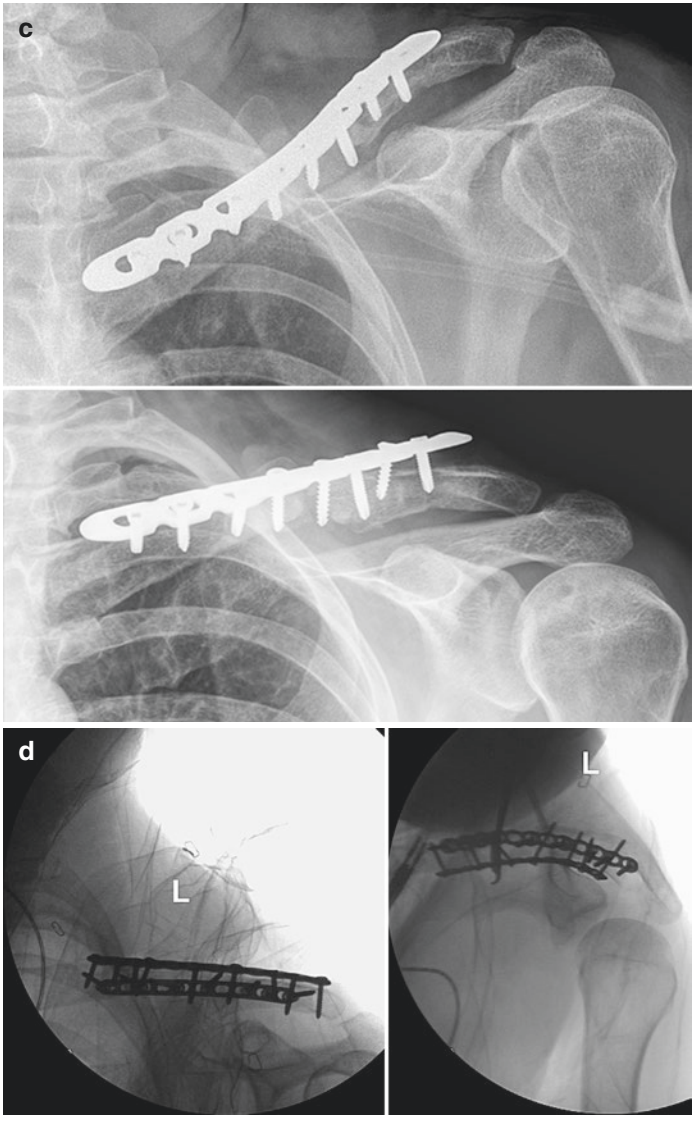


FIGURE 7.1 (continued)

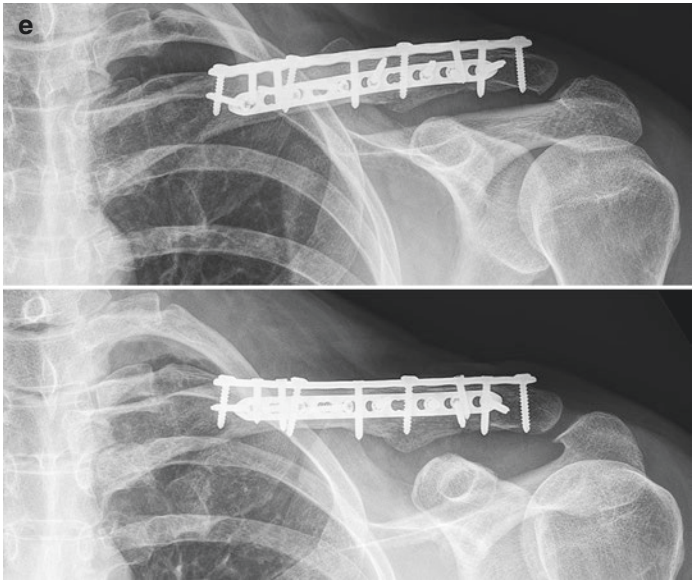


Figure 7.1 (continued)

Two weeks later, radiographic imaging demonstrated predictable progression of fixation failure. While an infectious etiology was suspected as the cause for her nonunion, standard infectious inflammatory markers were negative: WBC – 6.94, ESR – 5 mm/hour, and CRP <0.7 mg/dl. She remained afebrile with normal vital signs throughout her presentation. At this stage, with a benign-appearing wound, she was referred to us for further treatment. We recommended a single-stage surgical debridement and revision fixation. Prior to commencing surgery, we consulted the infectious disease service for assisted management of this patient as we anticipated the need to treat her injury as an infected nonunion.

She was admitted for surgery and underwent removal of previous hardware and formal irrigation and debridement with five tissue specimens (not swabs) taken from the nonunion site sent for microbiologic analysis, at the recommendation of infectious disease service. Each specimen was sent for

aerobic and anaerobic culture, and two of them were selected for additional mycobacterial and fungal culture. Her clavicle fracture was treated with revision open reduction and compression with dual plating, a technique with which we have had much success (Fig. 7.1d) [1]. Her wounds were closed over a drain, and she was placed on IV vancomycin and ceftriaxone empirically, at the recommendation of infectious disease, while we awaited the culture results. Although aerobic cultures at 5 days yielded no growth, multiple anaerobic cultures at 6 days grew *Propionibacterium acnes*. She received penicillin via a PICC line to complete a 6-week treatment course as an outpatient with regular follow-up visits.

After completion of her course of IV antibiotics, she transitioned to oral amoxicillin for suppression over the next 6 months until her left clavicle was clinically and radiographically united (Fig. 7.1e). At that time, she displayed no signs of continued infection, and the antibiotics were discontinued. She did not require any further surgical intervention for repeat debridement or hardware removal. At the last follow-up, 24 months after nonunion revision, she was without signs or symptoms of infection or hardware complication.

## Discussion

Although most operatively treated fractures do heal, some progress to nonunion. Open fractures and previous surgery are risk factors for development of infection. Infections should strongly be considered as a contributing factor of nonunion after operative treatment [2]. In the setting of infection, nonunions can be particularly challenging to treat [3].

Diagnosis of infection can be done preoperatively with standardized blood work looking for elevated markers of infection: serum white blood cell (WBC) count, C-reactive protein (CRP) level, and erythrocyte sedimentation rate (ESR) [4]. In one single-center retrospective study of patients presenting with nonunions, the probability of an infected nonunion with zero, one, two, and three positive tests were

19.6%, 18.8%, 56.0%, and 100%, respectively [5]. Patients who present with subclinical and indolent infected nonunions that are otherwise asymptomatic or "presumed aseptic" present a more unclear clinical picture that is complex and challenging. In this subset of patients, standardized inflammatory markers may not be elevated. Thus, it is difficult to diagnose infection in these patients prior to revision surgery [5–7]. Intraoperative isolation of one or more pathogens from tissue from the nonunion site remains the most reliable method for diagnosis of infection [4]. While most bacterial pathogens grow within 2–4 days in the microbiology laboratory, *P. acnes* and other less-common pathogens can take significantly more time, and sometimes special growth conditions, to be detected. The prospect of molecular detection of orthopedic pathogens may someday render current culture-based techniques obsolete, but for now intraoperative culture remains the gold standard for pathogen detection in these orthopedic cases.

There is debate in the joint arthroplasty literature between single-stage and two-stage treatment of infections [4, 6]. As standardized guidelines do not exist for infected nonunions, applying this treatment algorithm to clearly infected nonunions (symptomatic infection with systemic sepsis or clinical signs of infection such as a draining wound or communicating sinus), a two-stage surgical protocol is often recommended [4, 6, 8–10]. This involves the initial procedure for removal of hardware, obtaining cultures and aggressive surgical debridement. Fracture stability contributes to bony union and eradication of infection in the setting of low-virulence infections [11–13]. Temporary stabilization can sometimes be utilized depending on the anatomic location if stability can be achieved safely while the infection is treated. In the lower extremity, temporary stability can be achieved through an external fixator or an intramedullary device coated with antibiotics. Adjuvant antibiotics can be delivered at the surgical site with various drug delivery systems as well. Systemic antibiotics, administered parenterally or orally, targeted toward the offending organism(s) are generally prescribed for

4–6 weeks [4, 6]. Once the antibiotic course is complete, the subsequent stage of definitive fixation with management of bony defects may be performed as long as no evidence of infection remains [8–10].

For patients without a history or clinical signs of infection, a single-stage procedure can be utilized for debridement and repair of the nonunion [2, 7, 14]. Incidence of positive intraoperative cultures in patients with a history of surgery or open fracture at the time of definitive surgery has been reported at 20% [2]. In their series, Olszewski et al. recommend intraoperative cultures for all patients undergoing revision surgery, regardless of the clinical presence of infection. In a similar series, Amorosa et al. reported positive intraoperative cultures in 28.7% of patients with diaphyseal nonunions. Recently, success has been shown in treating infected nonunions with single-stage irrigation and debridement with stable fixation, with or without bone grafting, in the same surgical procedure. In a study by Olzewski et al., 78% of nonunions who were culture positive healed after a single surgery. Arsoy et al. reported similar rates of union at 84% after the index nonunion surgery for patients who were culture positive. In both series, patients were treated postoperatively with culture-specific antibiotics for an appropriate period of time.

General treatment principles for infected nonunions include aggressive surgical debridement of nonviable tissue and necrotic or infected bone, intraoperative cultures for diagnosis, stable fixation, and proper management of bone defects [10]. Infectious disease consultation is recommended to assist with diagnostic management and antibiotic treatment and monitoring.

At our institution, we generally withhold all antibiotics for at least 2 weeks prior to revision nonunion surgery in order to optimize the sensitivity of intraoperative cultures [4]. At the time of surgery, optimally five intraoperative samples are taken from the infected nonunion site to be submitted for aerobic and anaerobic bacterial culture to maximize success of obtaining a diagnosis. This derives from the recommendations of the prosthetic joint infection

(PJI) literature [4]. Generally, two or more positive cultures make infection significantly likelier than one or fewer. Antibiotic therapy is recommended if two or more cultures isolate the same organism as per the Musculoskeletal Infection Society and International Consensus Group criteria for PJI [4]. The likelihood of infection is quite low in the setting of a single positive intraoperative culture without other positive indicators [15]. Therefore, a single positive culture can be ignored if the organism is of low virulence or likely to be a contaminant from skin [4, 6]. However, in the setting of a highly virulent organism such as MRSA and gram-negative organisms or with clear evidence of infection grossly or from systemic lab markers, treatment may well be indicated at the discretion of the orthopedic and infectious disease teams [4, 6]. We treat infections diagnosed after single-stage revisions of presumed aseptic nonunions with hardware retention and a high-intensity IV or oral course of antibiotics for the appropriate duration depending on the organism, followed by oral antibiotic suppression at lower doses until clinical and radiographic union as defined by the surgeon. We define clinical union as absence of pain at the fracture site and radiographic union as restoration of sufficient structural cortical continuity seen on x-ray or confirmed using CT.

**Clinical Pearls**

1. Open fractures and history of previous surgery are risk factors for infection.
2. Infection should always be considered in the workup of a fracture nonunion.
3. Inflammatory markers, serum white blood cell [WBC] count, C-reactive protein [CRP] level, and erythrocyte sedimentation rate [ESR], can be used to diagnose infection; however the gold standard remains tissue culture from the nonunion site.

4. Principles for management of "infected" nonunions include:
   (a) Aggressive debridement of infected and nonviable soft tissue and bone.
   (b) Obtaining intraoperative tissue for culture, even without clinical signs of infection due to reported rates of "surprised infection." We recommend five to six samples of tissue sent for aerobic and anaerobic culture. Two mycobacterial and fungal cultures are recommended if there is clinical concern for unusual nonbacterial organisms.
   (c) Reduction with compression across the nonunion and stable fixation – we have published 100% union rates in clavicles even in the setting of infection using dual orthogonal plating of clavicles [16].
   (d) Management of bony defects with autograft or allograft bone.
   (e) IV or oral antibiotics directed against infectious organism for 4–6 weeks, followed by oral antibiotic suppression until clinical union – monitored and directed by infectious disease specialists.
5. Not all infected nonunions can be treated with a single surgical procedure. Clinical sepsis, draining sinus, and frank purulence are all signs of overt infection that should likely be treated with a staged procedure and temporary stabilization, if necessary.
6. Presumed aseptic nonunions treated with a single surgical procedure can still achieve high union rates even in the presence of infection with the appropriate management and close follow-up.
7. The ultimate decision regarding surgical management should be made by the orthopedic surgeon with appropriate consultation from other services including infectious disease (culture and antibiotic management) and plastic/microvascular surgery (soft tissue coverage needs).

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# Chapter 8
# Nonoperative Management of the Diabetic Foot Infection

**Ashley Shoultz and Tejas T. Patel**

## Case

A 60-year-old male with a history of type II diabetes mellitus presents with a wound at the plantar aspect of the base of the right heel. He has a history of wounds and first noticed this wound 2 days ago after a round of golf in a new pair of shoes. He denies any fevers or chills. He has not noted an increase in his blood glucose levels.

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J. Reznicek et al. (eds.), *Musculoskeletal Infections*,
https://doi.org/10.1007/978-3-030-41150-3_8

## Physical Exam

Temperature 38.5 °C; pulse 85; respiration 11; blood pressure 137/70. HEENT: unremarkable. Cardiac: regular rate and rhythm. Abdomen: unremarkable. Extremities: loss of hair below knees, dry cracked skin bilaterally to feet. Mild pitting edema to mid-calf. Chronic venous stasis changes to the lower leg. 2+ dorsalis pedis and posterior tibial pulses. Insensate to 5.07 mm Semmes-Weinstein monofilament throughout the foot. Ulceration to the plantar aspect of the heel measuring 6.2 cm × 5.5 cm. The ulcer has granulation tissue at the base through about 50% of the wound; the rest has fibrinous tissues. Surrounding the wound is some hyperkeratotic skin. There is minimal surrounding erythema and mild serous drainage.

## Laboratory Findings

- WBC 11,600
- Glucose 156 mg/dL
- Hemoglobin A1c 7.8%
- Albumin 4.5 g/dL
- BUN 25 mg/dL
- Creatinine 1.2 mg/dL
- ESR 16 mm/hour
- CRP 1.1

Images of the wound on initial presentation are presented in Fig. 8.1.

The patient was diagnosed with a diabetic foot ulceration and treated by a multidisciplinary team including an orthopedic surgeon, a wound care specialist, and his primary care physician. It was determined that the patient had a superficial infection surrounding the ulceration due to some erythema and ulcerations. He was treated empirically with a 7-day course of clindamycin after consultation with an infectious diseases specialist. MRI and x-rays did not show any evidence of deep infection. An ankle-brachial index

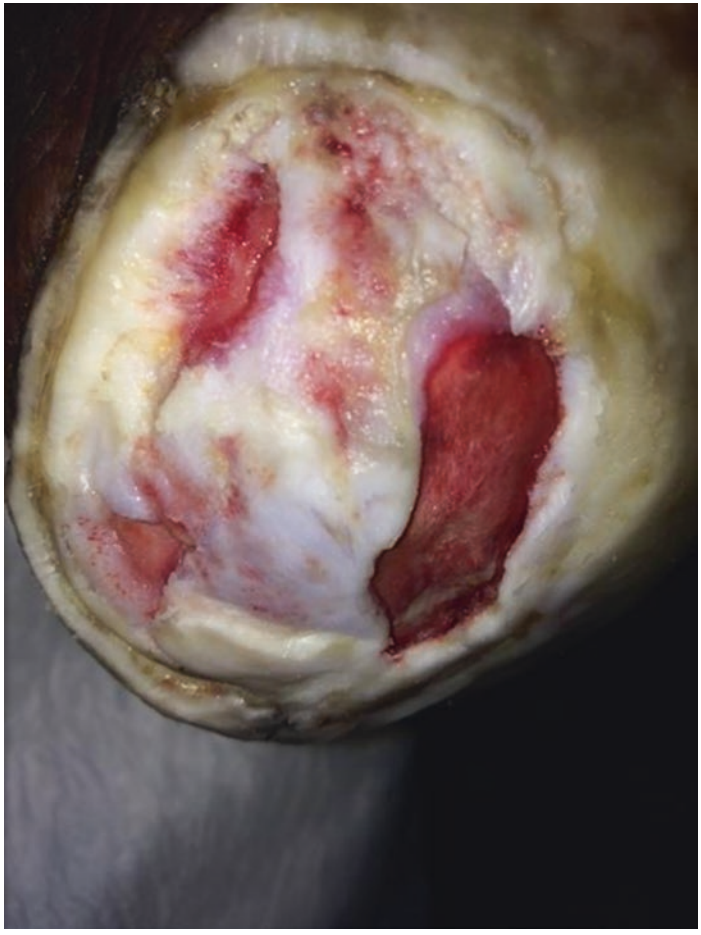


Figure 8.1 Picture of heel ulceration of day of presentation. Note the red beefy granulation tissue throughout the base with area of white fibrinous tissue. It also has surrounding hyperkeratotic skin at the edges

was obtained to confirm adequate blood flow and was 0.95; therefore, vascular surgery consultation was not obtained. The patient was treated with total contact casting with resolution of the ulceration. He was subsequently referred to an orthotist for molded diabetic inserts and extra-depth shoes to

prevent recurrence. The primary care physician worked with the patient to lower his blood glucose levels and improve his hemoglobin A1c.

## Discussion

### *Epidemiology*

Diabetes is known to affect approximately 9% of the population worldwide, and of this population 25% will develop a foot complication, most often being an ulceration. Diabetic foot infection results in 40–60% of those with an ulceration and is a leading factor in limb amputation [1, 2]. Infection can result from a break in the skin due to a neuropathic ulcer, in which bacteria can enter and travel downward into the deeper tissues and/or bone causing cellulitis, osteomyelitis, and sepsis. Infection risk is increased when the patient has a chronic wound, recurrent wounds, previous amputation, positive probe-to-bone test, neuropathy, renal disease, and history of walking without foot protection [2].

### *Pathophysiology of Diabetic Foot Ulceration*

A diabetic foot ulceration occurs secondary to the multiorgan dysfunction that arises from chronic hyperglycemia. Neuropathy, vasculopathy, structural changes, and immunosuppression are strongly associated with ulcer formation and infection. Neuropathy involves the sensory, autonomic, and motor systems. Sensory neuropathy results in loss of protective sensation and blunts the pain response to local tissue trauma, thereby increasing risk of wounds developing and progressing prior to initial presentation [3]. Autonomic dysfunction impairs normal secretory function of the glands in the feet causing dry, cracked skin which is susceptible to fissuring. This fissuring can serve as portal for bacteria and infection [4]. Motor neuropathy causes muscle imbalances

contributing to claw toes and equinus contractures. These deformities can increase plantar pressure across the metatarsal heads and lead to ulcerations, particularly in the forefoot [5]. Vascular insufficiency leads to local tissue ischemia and can contribute to necrosis of marginally perfused tissues. Marginally perfused tissues also have diminished healing potential. Deformity increases plantar pressures across the foot and in the setting of neuropathy increases risk of ulceration formation [6].

## *Clinical Findings*

On exam, the practitioner should note the size and shape of ulcerations. Pictures can be helpful to monitor progression of the wound. An alternative is to make a tracing of the wound and record measurements of the wound. It is essential to note the depth of the wound, which can be quantified by a numeric measurement or extension to exposed structures. A wound that probes to bone is assumed infected until proven otherwise [7]. The extent of autonomic neuropathy can be assessed by noting hair pattern on the lower extremity and appearance of skin. Sensory neuropathy is commonly assessed using a monofilament. Studies suggest using the 10-gram or 5.07 Semmes-Weinstein monofilament as the minimal threshold for protective sensation [8]. Deformity and bone prominences should be noted particularly in the area of the ulceration as they can contribute to the formation of ulcers, particularly on the plantar aspect of the foot.

Infection may be difficult to diagnose secondary to the reduced host immune response. Decreased arterial sufficiency is common in the diabetic patient and may result in reduced erythema and induration to the infected wound. Pain may be lacking due to neuropathy. Systemic signs such as increased white blood cell count and erythrocyte sedimentation rate and fever may be absent. The clinician should evaluate for secondary signs of infection such as foul or increased drainage, poor quality or friable granulation tissue, or under-

mined edges [1]. Obtaining a superficial wound culture of a diabetic ulcer is controversial. Chronic wounds are colonized with a myriad of bacteria causing superficial wound cultures to be unreliable in finding a causative organism. Still, cultures may be useful in discovering whether or not a prominent bacterium is drug resistant. Diabetic foot ulcerations commonly present with associated cellulitis. It is generally diagnosed based on physical exam findings including erythema, increased pain, and drainage combined with lab values such as elevated white blood cell count, ESR, CRP, and loss of glucose control. Tissue or bone cultures are more sensitive as they are more likely to contain a sole causative organism and they are essential when treating a deeper infection [1]. Mild infections or infections in patients who are antibiotic naïve are more likely to have one or two bacteria, typically gram-positive cocci such as *Staphylococcus* spp. More developed infections may be polymicrobial and include gram-negative rods and anaerobes [1].

## *Management*

Management of the diabetic foot ulcer infection requires a multidisciplinary approach. The team should include a podiatric/orthopedic surgeon, a vascular surgeon, an infectious diseases specialist, a certified wound care specialist, and either an endocrinologist, internist, or family practitioner. Treatment should cover a myriad of aspects including glycemic control, vascular optimization, offloading, topical wound care, surgical debridement, and infection control [1].

## *Glycemic Control*

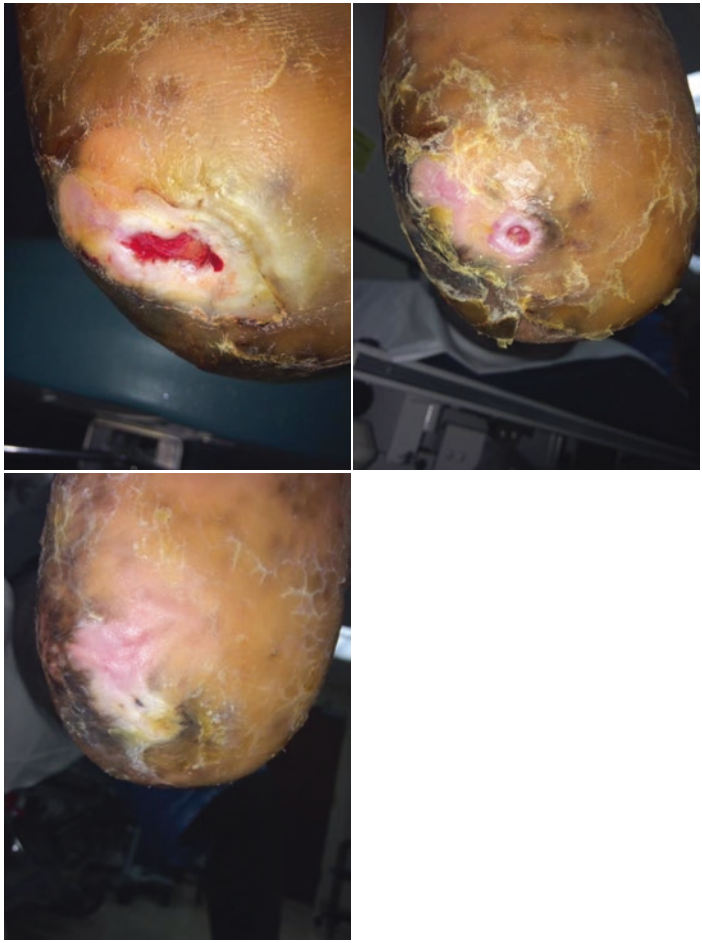
Poor glycemic control is the primary cause of the development of neuropathy in the diabetic. High glucose levels result in leukocyte dysfunction and impaired endothelial function which can result in a poor response to infection. Patients with

elevated hemoglobin A1C levels have been known to have a normal white blood cell count. Improving glucose levels will improve the immune response to infection [9].

## *Offloading*

Offloading is essential for both prevention and the treatment of diabetic foot ulcers. Offloading works by redistributing the pressure on the plantar surface of the diabetic foot. Although there are many options for offloading (bedrest, crutches, wheelchair, surgical shoes, foam dressings), the most effective is through total contact casting (TCC). TCC results in equalizing pressure throughout the plantar surface of the foot, so that direct pressure to the wound site is reduced. Pressure can be further reduced by adding an offloading base to the plantar surface so that little to no pressure is applied to the wound during ambulation. There have been studies showing that TCC is superior to removable cast walkers due to compliance being low when patients are able to remove the walker. There are contraindications to using TCC, such as deep space infection or gangrene, sepsis, excessive edema, and moderate-several peripheral arterial disease. One should also take caution if the patient has a history of instability or balance issues [9]. Studies seem to indicate that the total contact cast is effective at reducing forefoot pressure. Some studies have shown that the pressure is transferred to the cast and lower leg, and others have shown that the pressure is transferred to the cast and heel. While forefoot ulcerations tend to respond better compared to heel ulcers, TCC is still effective in treating heel ulcerations [10, 11]. Figures 8.2–8.4 show near resolution of a heel ulcer with total contact casting.

In those patients who cannot receive total contact casting, a modified offloading can be made using felted foam dressings. Securing the felted foam dressing directly to the skin around the ulceration is essential to ensure proper offloading during ambulation. There is also an array of boots and shoes that can help offload various aspects of the foot.



FIGURES 8.2–8.4 Pictures of the diabetic foot ulcer from Fig. 8.1 undergoing TCC changing biweekly with appropriate antimicrobial foam dressing. Total course of treatment 3 months

## *Topical Wound Management*

Bedside debridement of the wound and the surrounding callous is the first step in managing a wound related to diabetes. A hyperkeratotic callous is often surrounding the ulcer sec-

ondary to the drying effect of the autonomic nervous system dysfunction in addition to the body's response to minor repetitive trauma. This response builds a callous which is meant ultimately to defend from outside trauma but inadvertently increases the plantar pressure resulting in ulceration. The callous surrounding the central ulceration prohibits new epithelium from migrating from the edges. Debriding the callous down to healthy epithelium is essential in allowing the migratory cells to flourish and to decrease the plantar pressure. Debridement of the wound itself has several functions including removal of bacteria and biofilm and the stimulation of growth factors by restarting the wound healing cascade. Debridement can be performed with a variety of instruments including scalpel, curette, rotary files, and ultrasonic contact debriding machines. Every effort should be made to pare the callous to a smooth rounded edge, attempting to reduce any micro pressure points [9].

After topical debridement of the ulceration and surrounding nonviable tissue (which may need to be done serially), the clinician may choose an appropriate cover dressing. Dressing options have increased over the years, providing the clinician with a wider variety of choices. A dressing should be chosen based on the wound needs, and the clinician should follow basic moist wound healing principles. Factors to consider include wound exudate level, bioburden, and projected dressing change frequency. Alginates and foams are usually appropriate for the diabetic ulcer as drainage level is generally high. Antimicrobial versions of these dressings can be chosen if bacteria levels on the surface of the wound remain high. Some dressings are indicated for up to 1, 3, or 7 days. It is important to be cognizant of manufacturer's guidelines when choosing a topical dressing. For diabetic foot infections in which the infection has been eradicated and appropriate topical care has been induced but the wound remains stalled, more advanced therapies may be utilized. Advanced therapies may include negative pressure wound therapy, recombinant human platelet-derived growth factor, cellular tissue products, and hyperbaric oxygen therapy [12]. Once the wound has been

healed, the patient should be referred to an orthotist to fashion custom molded inserts to help prevent recurrence.

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# Chapter 9
# Operative Management of the Diabetic Foot Infection

**Tejas T. Patel**

## Case

A 58-year-old female with history of type II diabetes presents with a wound at the plantar aspect of the base of the left fifth metatarsal. She first noticed it after a trip to the theme park with her grandchildren, about 11 weeks prior. It initially presented as a small wound with a surrounding blister which progressively expanded to a large ulceration. She had seen a wound care specialist who recommended she apply a salve to debride the wound and promote healing, as well as non-weight-bearing. She had been compliant with dressing changes but had continued to walk on it due to balance problems and concerns for falls.

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J. Reznicek et al. (eds.), *Musculoskeletal Infections*,
https://doi.org/10.1007/978-3-030-41150-3_9

## Physical Exam

Temperature 38.7 °C; pulse 91; respiration 15; blood pressure 145/79. HEENT: unremarkable. Cardiac: irregularly irregular. Abdomen: unremarkable. Extremities: loss of hair below knees, dry cracked skin bilaterally to feet. 2+ pitting edema to mid-calf. Chronic venous stasis changes to the lower legs. Faintly palpable dorsalis pedis and posterior tibial pulses. Insensate to 5.07 mm Semmes-Weinstein monofilament throughout the left foot. Ulceration at the base of the left fifth metatarsal measuring 5 cm × 3 cm. The ulcer has a necrotic base surrounded by fibrinous tissue. Surrounding erythema throughout the lateral foot and ankle with "dishwater"-type drainage from the wound.

## Laboratory Findings

- WBC 15,600 with 85% neutrophils
- Glucose 314 mg/dL
- Hemoglobin A1c 10.1%
- Albumin 3.1 g/dL
- BUN 25 mg/dL
- Creatinine 2.7 mg/dL
- ESR 99 mm/hour
- CRP 7.0

Images and radiographs of the foot are presented in Figs. 9.1 and 9.2.

Based on clinical evaluation including physical exam findings as well as laboratory values, this patient was diagnosed with an infected diabetic foot ulceration. She was treated by a multidisciplinary team including a vascular surgeon, an orthopedic surgeon, an infectious diseases specialist, and an endocrinologist. Based on radiographs and physical exam, it was determined that the infection involved the bone. Severe osteolysis indicated that she had dead bone in the fifth metatarsal. Antibiotics were held as the patient was hemodynamically stable until urgent operative intervention.

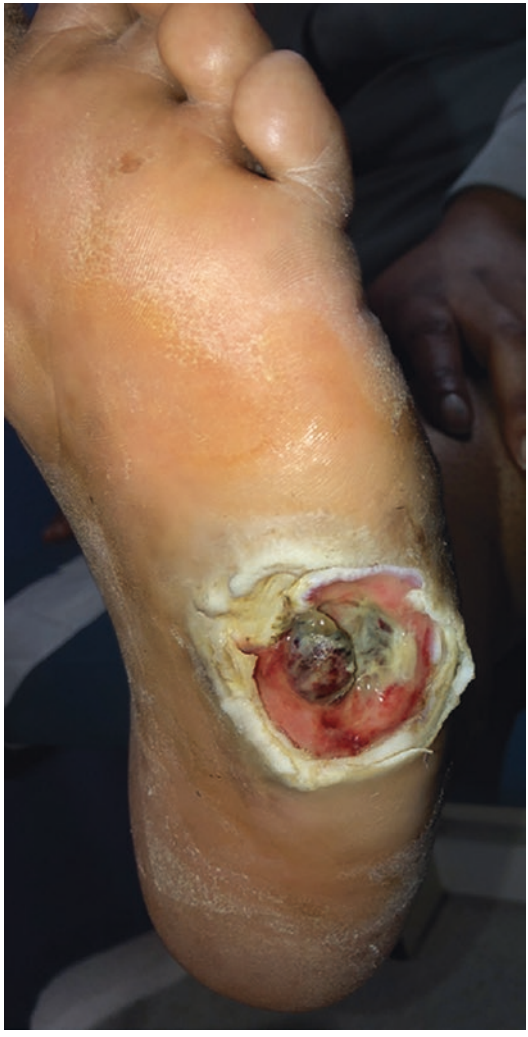

FIGURE 9.1 Clinical photograph of the left foot. Ulceration at the base of the fifth metatarsal with necrotic base and surrounding macerated tissues

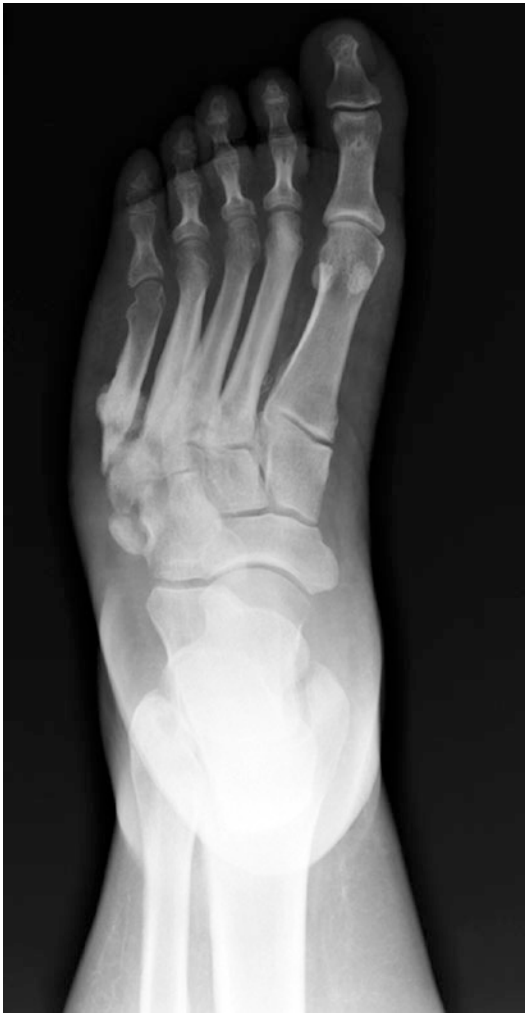

FIGURE 9.2 Anteroposterior radiograph of the left foot. Severe bone fragmentation and osteolysis through the base of the fifth metatarsal with areas of sclerosis

Treatment of the infection involved resection of the fifth ray to obtain source control and culture-specific antibiotics for 6 weeks based on intraoperative cultures. Infectious diseases was consulted to determine appropriate antibiotic choice and length of treatment. They followed the patient post-discharge for proper monitoring for toxicity and side effects of the antibiotic regimen. Given the reduced pulses on examination, an ankle-brachial index was obtained and found to be 0.72 and toe-brachial index was 0.5. This indicated she had peripheral vascular disease and diminished perfusion to the limb; therefore, vascular surgery was consulted for revascularization. Due to her poor glucose control, endocrine was consulted during her inpatient stay to develop an appropriate glucose control regimen. A nutritionist educated the patient about the appropriate diet to maintain glucose control and increase protein intake to assist with healing. Once she was healed, she was referred to an orthotist for custom molded diabetic inserts and extra-depth shoes to prevent recurrence.

## Discussion

### *Background*

Diabetes mellitus and associated hyperglycemia cause significant end-organ damage in multiple organ systems. Foot disease develops secondary to neuropathy, peripheral vascular disease, biomechanical dysfunction, deformity, diminished wound healing capacity, and immunosuppression. About 58% of diabetic foot ulcerations (DFUs) have an associated infection on initial presentation [1]. This disease process is associated with significant morbidity and mortality. A European study found that about 5% of patients with DFU required amputation within 1 year [2]. Five-year mortality rate for neurotrophic ulcerations is reportedly as high as 45% [3]. It is rare for the ulcer and infection to be the attributable cause of death; rather, DFUs are surrogate indicators of severe end-organ damage in patients with diabetes.

## *Pathophysiology*

A DFU is the result of damage to multiple organ systems. Neuropathy is a major risk factor for DFU formation. It affects the sensory, autonomic, and motor systems. Sensory neuropathy diminishes the capacity of the foot to recognize damage and trauma to the foot. Subsequently, even minor trauma to the foot can progress to large and deep ulcerations. Autonomic dysfunction reduces physiological secretions that maintain integrity of the integumentary system resulting in dry cracked skin that can then serve as an entry point for bacteria and infection. Motor neuropathy causes muscle imbalance which leads to claw toes, hammer toes, prominent plantar metatarsal heads, and contractures. These deformities can cause abnormal pressure points across the foot increasing risk of ulcerations and wounds [4].

Peripheral vascular disease and immunosuppression are often associated with diabetes mellitus. Hyperglycemia causes sclerosis and calcification of both small and large vessels leading to decreased perfusion. Without adequate blood flow, wounds do not heal well and the immune response at site of infection is impaired. Hyperglycemia also decreases T-cell response, neutrophil function, chemotaxis, and phagocytosis [4, 5]. In the setting of poor vascularity and immunosuppression, pathogens can invade the body through breakdown in the skin and cause a diabetic foot infection, which occurs in about 50% of all diabetic foot ulcerations [6].

## *Clinical Evaluation*

The key to treating this patient is to recognize the severity of the wound/infection, treat the wound/infection in accordance with the severity, and address any modifiable risk factors to promote healing and prevent future ulcerations and wounds. The severity of the wound and infection is determined based on physical exam findings, symptoms, lab work, and imaging.

Erythema, drainage, and fluctuance are common findings in the setting of infection. Sometimes increased pain is associated with infection; however, if there is moderate to severe neuropathy, patients may experience minimal to no pain. Rapid ascending erythema is a sign of aggressive infection and warrants a prompt surgical consultation and initiation of intravenous antibiotics. Drainage can vary from frank purulence to a more murky serous fluid described as having a "dishwater" appearance. Increasing drainage is generally a sign of infected ulceration. All wounds should be gently probed to determine depth and to detect possible exposed bone. Exposed bone is considered osteomyelitis until proven otherwise, with a positive predictive value between 59% and 89% for osteomyelitis [7].

Common systemic symptoms associated with infection include fever, chills, anorexia, and malaise. Septicemia and septic shock can occur with infected diabetic ulcerations; however, it is relatively rare. Blood work should include a basic metabolic panel, complete blood count with differential, blood cultures, hemoglobin A1c, as well as an erythrocyte sedimentation rate and a C-reactive protein level, which can be helpful to monitor progression of treatment. Often, the onset of infection is associated with loss of glycemic control in diabetics. Albumin, prealbumin, and total lymphocyte count can help assess nutritional status.

A major component of the workup should also include assessment of modifiable risk factors. This will guide toward interventions that will help the patient heal the ulcer, resolve infection, and hopefully prevent future recurrence. Primary risk factors for ulcer formation and wounds in diabetics include peripheral neuropathy, inadequate blood flow, deformity, and poor shoe fit. Peripheral neuropathy is most easily and reliably assessed using the 5.07 mm Semmes-Weinstein monofilament test and 128-Hz tuning fork. If a patient cannot feel these, it indicates they have loss of protective sensation. Motor neuropathy can result in equinus contracture and hammer toes which increases pressure under the forefoot and toes. On physical examination, vascular status

is determined by palpating pulses (dorsalis pedis, posterior tibial) and examining the capillary refill in toes. However, presence of pulses does not always exclude peripheral vascular disease. If there are any concerns about asymmetric or reduced pulses, prolonged capillary refill, or peripheral vascular disease; noninvasive arterial studies, such as ankle-brachial index and toe pressures, should be obtained. An ankle-brachial index below 0.9 or above 1.4 is considered abnormal and warrants vascular consultation. Calcification of arteries can artificially elevate ABIs but distorts toe pressures less. A toe-brachial index below 0.7 warrants vascular consultation [8].

Due to the combination of motor neuropathy causing muscle imbalance and sensory neuropathy causing Charcot arthropathy, diabetics often get various foot deformities. Deformity of the foot increases plantar stress on the foot. Some studies have suggested that those who develop diabetic foot ulcers had increased shear stress on the plantar aspect of the foot and this may contribute to ulcer formation [9]. Atrophy of intrinsic foot muscles can cause hammer and claw toe deformities that can lead to callus and ulcer formation on the dorsal proximal interphalangeal joints. Clawing of toes can make the metatarsal heads more prominent on the plantar aspect of the foot and combined with equinus contracture, this puts them at risk for a plantar forefoot ulceration.

Imaging helps determine the extent of infection and also helps with surgical planning. Initial imaging of choice is an x-ray of the affected body part. Lucencies or erosions on x-rays indicate the presence of necrotic bone. MRI is the most specific and sensitive test to determine osteomyelitis and usually the best test to evaluate for abscess in this patient population. CT scans require iodinated contrast to evaluate for abscess which can be nephrotoxic, especially in patients with preexisting chronic renal insufficiency. In addition, CT scans poorly detect early osteomyelitis [10].

## *Treatment*

Diabetic foot infections are best managed by a multidisciplinary approach given the confluence of factors that contribute to this pathology. From a systemic standpoint, associated symptoms such as fever, renal failure, sepsis, and shock should be medically treated. Sepsis and shock are indications to start immediate broad-spectrum antibiotics in addition to standard resuscitation measures. A good glucose control regimen should also be established.

Surgical treatment can play a critical role in source control and acquisition of deep cultures. Adequate source control requires debridement of all necrotic tissues including soft tissues and bone. Sometimes multiple rounds of debridement are required to get to a healthy wound bed. Amputations may be necessary with severe bone and soft tissue infections. Deep cultures help identify pathogenic organisms causing the infection and help develop ideal antibiotic regimen [11]. Unless the patient is unstable, systemic broad-spectrum antibiotic should not be administered immediately, because antibiotic therapy prior to acquisition of appropriate deep cultures can lead to false-negative culture results. Duration of antibiotic therapy is controversial. A study comparing a 6-week course versus a 12-week course found no statistically significant difference in recurrence rate at 1 year [12].

Once the infection is cleared and the ulcer has resolved, measures can be taken to reduce recurrence. There have been randomized controlled trials demonstrating that custom diabetic inserts in appropriate shoes can reduce recurrence rate of diabetic foot ulcerations. However, data has not been as supportive that shoes and insert combinations decrease initial ulcer formation [13, 14]. Sometimes severely deformed feet cannot fit appropriately into a shoe. In these cases, a Charcot restraint orthotic walker (CROW) boot may be helpful to appropriately off-load pressure points. Surgical correction of the deformity may also be warranted [11].

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# Chapter 10
# Onychomycosis

**Seth J. Schweitzer**

## Abbreviations

| | |
|---|---|
| DLSO | Distal lateral subungual onychomycosis |
| DNA | Deoxyribonucleic acid |
| EO | Endonyx onychomycosis |
| KOH | Potassium hydroxide |
| Nd:YAG | Neodymium-doped yttrium aluminum garnet |
| PAS | Periodic acid-Schiff |
| PCR | Polymerase chain reaction |
| PDT | Photodynamic therapy |
| PSO | Proximal subungual onychomycosis |
| SDA | Sabouraud dextrose agar |
| SWO | Superficial white onychomycosis |
| TDO | Total dystrophic onychomycosis |

## Case

A 38-year-old healthy male presents with chief concern of an abnormal right great toenail and abnormal left great and second toenails. Patient relates the right great toenail has

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J. Reznicek et al. (eds.), *Musculoskeletal Infections*,
https://doi.org/10.1007/978-3-030-41150-3_10

been thickened and discolored for 5 years, but the left two affected toenails have changed more recently, within the previous 2 years. He also has noticed mild redness, scaling, and itching in the first and second interspaces of his left foot. He relates using an over-the-counter topical antifungal spray which helped for a short period of time, but did not eradicate the problem. Patient denies any specific history of trauma. He works in a factory, stands the majority of the time, and is required to wear steel toe boots. He relates mild tenderness on direct pressure to the right great toenail due to its thickness but is more concerned about the changes occurring to the left two toenails which he feels may be spreading. He feels embarrassed when exposing his feet at the gym or on vacation.

On examination his neurovascular status is intact. The right great toenail shows significant thickening, 3–4 mm. It is dystrophic, hypertrophic, discolored, and mildly incurvated at the medial and lateral nail borders with subungual debris. These findings involve 100% of the right great toenail. Mild tenderness is noted on direct palpation and there is no evidence of soft tissue infection. The left great and second toenails reveal discoloration, dystrophy, and onycholysis with subungual debris and hyperkeratosis. These findings involve 30% of the distal aspect of the nail plates. No tenderness is noted on the left side. There is localized redness and scaling to the first and second interspaces of the left foot.

Clippings of the offending nails sent for laboratory examination using PCR (polymerase chain reaction) detected the dermatophyte *Trichophyton rubrum.* Baseline liver function tests ordered were within normal limits.

He was placed on oral terbinafine 250 mg daily for 12 weeks and topical efinaconazole 10% solution once daily to affected nails for 48 weeks. He was also prescribed a topical antifungal for the associated tinea pedis on his left foot. He followed up every 2 months for evaluation and nail debridement. He tolerated the oral medication well and was compliant with the treatment plan.

At 1 year following the start of treatment, the left great and second toenails showed marked improvement in the appearance of the nails with no evidence of disease. The interspaces of the left foot showed no abnormalities. The right great toenail showed no improvement with continued mild tenderness and an unfavorable appearance. At this time, patient opted for and received a total chemical matrixectomy of the right great toenail which healed uneventfully.

## Discussion

Onychomycoses, fungal nail infections, are common ailments presenting in the primary care, dermatologic, and podiatric communities. Toenails are more affected than fingernails. Patients more prone to this disease are those with peripheral vascular disease, diabetes, and other immunocompromising conditions, advanced age, sex (male>female), genetic predisposition, smoking, and trauma [1]. Athletes have a 2.5-fold increased risk in developing a fungal nail infection [2]. Creating a warm, dark, moist environment from shoe gear, socks, and sweating also increases the risk of developing nail infections.

Nail infections account for 50% of all nail disorders and are caused by dermatophytes, molds, and yeasts [3]. The dermatophyte *Trichophyton rubrum* accounts for the largest percentage of organisms causing onychomycosis, but other isolates from yeasts, non-dermatophytic molds, and bacteria may be playing a larger role than once suspected [4].

Patients present with nails that have become thickened, discolored, brittle, and/or detached from the underlying nail bed. The appearance of the nails has both medical and psychosocial implications. The evaluation of the patient starts with a thorough history and physical examination. Obtain the patient's pain level and how this condition may have affected their quality of life. Determine the time frame from when the nail has changed. Understanding the distribution pattern of

the affected nails may help the clinician come to a more accurate diagnosis. For example, if the hallux and fifth toenails are affected bilaterally, then the nail dystrophy may be attributed to shoe gear trauma or biomechanical forces. Once the information in the history and physical is obtained, laboratory testing is warranted to aid in the diagnosis and treatment plan.

Understanding the different types of onychomycosis will guide the practitioner to the most appropriate locations on the nail plate to obtain the specimen for laboratory testing. This may help reduce the amount of false-negative or false-positive results which erroneously alters the treatment plan. The different types of onychomycoses are as follows:

- Distal lateral subungual onychomycosis (DLSO), which is classified as the most common type, is appropriately named since the invasion originates from the distal and lateral margins of the subungual nail plate (Fig. 10.1).
- Superficial white onychomycosis (SWO) with the route of infection originating from the dorsal aspect of the nail plate (Fig. 10.2).

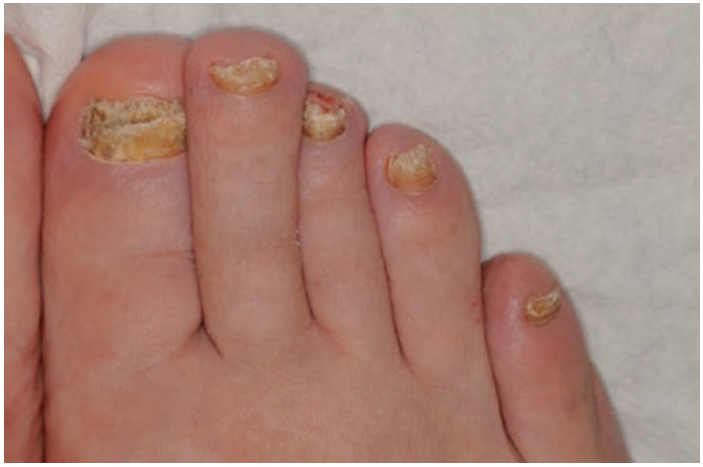

Figure 10.1 DLSO. Note the yellow discoloration, severe subungual hyperkeratosis, and onycholysis. (Image Reprinted from [5], with the permission of Springer International Publishing Switzerland 2017)

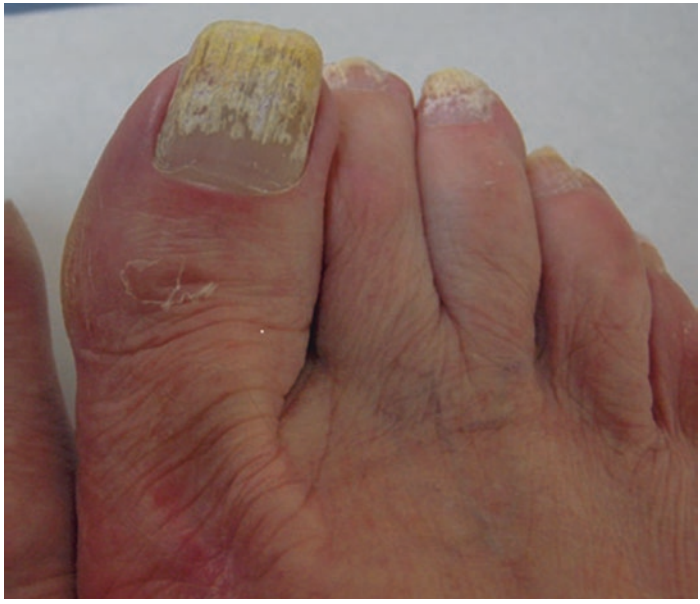

FIGURE 10.2 SWO. Note the yellow-white discoloration and crumbling of the nail surface. (Image Reprinted from [6], with the permission of Springer International Publishing Switzerland 2017)

- Proximal subungual onychomycosis (PSO) where the route of infection originates from the undersurface of the proximal nail fold and progresses distally (Fig. 10.3).
- Total dystrophic onychomycosis (TDO) which involves invasion of the entire nail plate and the surrounding periungual tissues (Fig. 10.4).
- Endonyx onychomycosis (EO), which is classified as a rare type; the invasion occurs at the superficial and deep portions of the nail plate and presents with a milky white nail plate discoloration. The infecting organism usually does not involve the nail bed nor does it present with lysis or subungual hyperkeratosis.

Prior to successfully treating onychomycosis, an accurate diagnosis [9] is necessary. Firstly, an appropriate sample of the

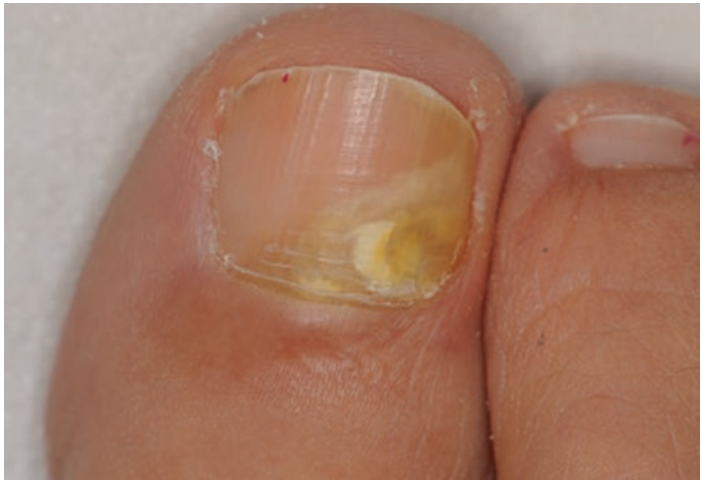

Figure 10.3 PSO. Caused by a non-dermatophytic mold with associated periungual inflammation. (Image Reprinted from [7], with the permission of Springer International Publishing Switzerland 2017)

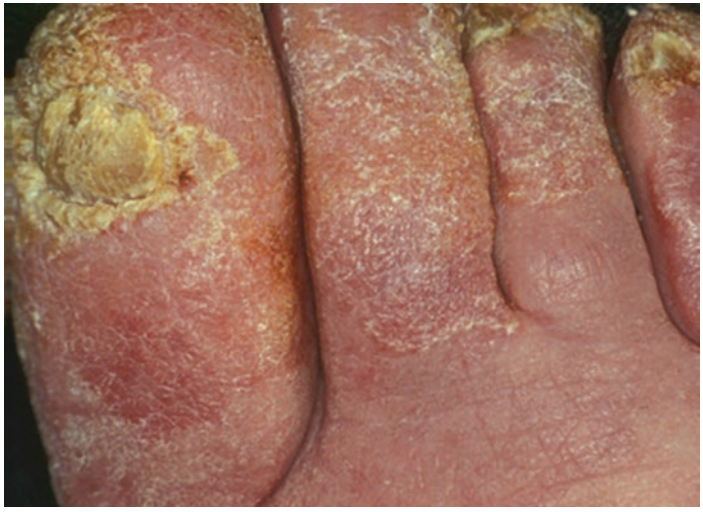

Figure 10.4 TDO. Note the involvement of the entire nail plate and the severe concomitant tinea pedis. (Image Reprinted from [8], with the permission of Springer International Publishing Switzerland 2017)

affected nail must be obtained. This can be achieved by, but not limited to, nail clipping, nail scraping, or punch biopsy. As in the case for DLSO, the specimen should be retrieved from the most proximal and lateral margins of the affected nail. It is important to note to avoid sending the most distal unattached portion of the nail for testing since this portion is more prone to result in false-negatives. In SWO, a nail scraping of the most affected and discolored aspect of the dorsal nail plate is appropriate. For suspected PSO, a 3 mm punch biopsy may be used to the dorsal plate to expose the underlying affected nail bed [6]. Once the nail specimen is obtained, laboratory testing can be ordered. The most common tests ordered are visual identification using microscopy with potassium hydroxide (KOH), mycologic culture medium with Sabouraud dextrose agar (SDA), periodic acid-Schiff (PAS) stain in histology, and molecular polymerase chain reaction (PCR). KOH is the oldest and most common test ordered. It has rapid screening and is inexpensive but is less sensitive than PAS and associated with false-negatives. SDA allows for identification of the organisms but is time-consuming at approximately 4 weeks, does not distinguish between pathogens or contaminants, and has a high rate of false-negatives. PAS is more sensitive than KOH, has an increased turnaround time, and may differentiate between the causative pathologies. PCR has rapid turnaround with increased accuracy but requires specialized equipment, increased cost, and false-positives due to the identification of noninvasive organisms as a consequence of the stability of deoxyribonucleic acid (DNA). Other methods of diagnostic testing include mass spectrometry, flow cytometry, and test strip. Mycological culture is considered the gold standard and the addition of the PAS stain helps decrease the high false-negative rate. This combination of testing is 94–98% sensitive [10].

Once the pathogen is identified, a treatment plan can be initiated. Onychomycosis can be treated with topical antifungals, oral antifungals, debridement of the nail, surgical removal of the nail (both temporary and permanent), and laser therapy. Success of treatment can be classified as mycologic cure, complete cure, and clinical cure. Mycologic cure is

defined as KOH and culture negative. Complete cure is defined as mycologic cure with a completely normal-appearing nail. Clinical cure is stated as 0% nail unit involvement, and clinical success as <5% and < 10% involvement [11].

Topical nail treatments are recommended for mild to moderate fungal nail involvement. Topical treatments, when indicated, are advantageous over oral medications due to their safety profile. The challenge with topical medication is compliance (daily application for up to 1 year), nail plate penetration, and lower than desired mycologic and complete cure rates. The three most common FDA-approved topical medications for onychomycosis available in the USA are ciclopirox 8% nail lacquer, efinaconazole 10% solution, and tavaborole 5% solution. Ciclopirox was the first topical approved in 1999. Efinaconazole and tavaborole were approved in the USA in June 2014 and July 2014, respectively. These two newer topical medications appear to have an advantage over ciclopirox due to their improved complete and mycologic cure rate. Urea 40% is another topical treatment option, when used as an adjunct to FDA-approved topical and oral medications, to be efficacious in the treatment of onychomycosis [12].

Oral therapies appear to be more efficacious than topical medication and are indicated for moderate to severe mycotic nail disease. Other advantages include shorter therapeutic times and improved patient compliance. The downside to oral medication includes possible adverse side effects, drug-drug interactions, increased risk of hepatotoxicity, and contraindications due to congestive heart failure. Terbinafine and itraconazole are the two FDA-approved oral medications to treat onychomycosis. Fluconazole has also been used as an off-label medication for fungal nail disease. It is recommended to get baseline hepatic function testing prior to starting oral medications and repeat testing in 6–8 weeks if recommended or warranted. Terbinafine is dosed at 250 mg/day, 6 weeks for fingernails, 12 weeks for toenails. Terbinafine may be pulse dosed 3 times at 500 mg/day for 1 week, repeated every 4 weeks. Itraconazole is dosed at 200 mg/day, 6 weeks for

fingernails, 12 weeks for toenails. Itraconazole may also be pulse dosed at 400 mg daily, 1 week on, 3 weeks off, two pulses for fingernails, three pulses for toenails. And lastly, fluconazole is dosed at 150–300 mg once weekly, 6–9 months for fingernails, 9–18 months for toenails.

Nail debridements and excisions are other treatment options. In attempts to provide a more timely solution to the subjective concerns of the patients, nail debridements have proven to reduce pain, improve appearance, and improve function. Unfortunately, debridement alone has been proven to be ineffective against eradicating a nail infection [13]. Total nail avulsion while undergoing medical treatment of the nail infection may not be the best course of action since this may lead to damage of the nail matrix, narrowing of the nail bed, and future ingrowing nail borders. Combinations of both topical and oral medications with mechanical debridements of the affected nails have been shown to be most effective. When these therapies fail to attain the desired outcome, permanent matrixectomies may be considered and warranted.

Device-based treatments for onychomycosis are currently active areas of research. They consist of lasers, photodynamic therapy (PDT), nonthermal plasma therapy, and UV light therapy [11, 14]. Only short-pulse neodymium-doped yttrium aluminum garnet (Nd:YAG) lasers have FDA approval for the treatment of onychomycosis. FDA approval for these laser devices are for "temporary cosmetic improvement" of onychomycosis, and since their approval standards are completely different than medications, they cannot be compared. Laser treatments also appear to have improved outcomes when used with adjunctive therapies. Further research continues to progress our knowledge of this topic. Until more solid evidence is obtained, topical and/or oral medications with or without mechanical debridement appears to be the most accepted standard of care.

The care of the patient with onychomycosis can be complex. Regaining the nail plate to the patient's perception of normal is extremely challenging. The clinician must understand that onychomycosis is more than a cosmetic complaint

by the patient, but rather a disease that may present with multiple underlying medical comorbidities. Clinical testing of the nail and accurately diagnosing the condition to construct the most effective treatment course is of utmost importance. Even once the diagnosis of onychomycosis is accurately obtained, discussing realistic expectations regarding clinical and cosmetic improvements with the patient is imperative. Today, clinicians can have a successful impact on improving the quality of life of these patients due to an abundant array of treatment options, whether monotherapy or combination therapy, to aid in the management of onychomycosis.

**Clinical Pearls**

1. A detailed history and physical examination is important in narrowing down a potentially extensive list of differential diagnoses.
2. Understanding the different types of onychomycosis, properly obtaining a nail specimen for laboratory testing, and confirming the diagnosis of onychomycosis.
3. Treating by combining both oral and topical medications in conjunction with mechanical debridement, when appropriate, is most effective.

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# Chapter 11
# Osteomyelitis of the Maxillofacial Region

**Daniel R. Hawkins and Robert A. Strauss**

## Case #1: Chronic Suppurative Osteomyelitis

A 67-year-old female with a history of hypertension and smoking was referred to the oral and maxillofacial surgery (OMFS) clinic for evaluation of an infection after having a dental extraction approximately 6 months earlier by her dentist due to a long history of pain and intermittent swelling. She noted that after the extraction, she still had constant pain and reported back to her initial provider who completed an in-office debridement with a short course of oral (PO) amoxicillin. She reported her constant pain persisted and she continued to experience intermittent swelling over the next several months. She was then referred to the OMFS service for continued exposed bone in the area. In the days preceding the appointment, she reported that the area began to produce purulent drainage. She also reported subjective paresthesia in the distribution of cranial nerve $V_3$ on the right. Extraoral trigeminal neurologic exam demonstrated level A through C

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J. Reznicek et al. (eds.), *Musculoskeletal Infections*,
https://doi.org/10.1007/978-3-030-41150-3_11

nerve testing was intact but with subjective paresthesia. She did have moderate swelling near her mandibular angle although the inferior border of her mandible was still palpable, indicating that there was no fascial space infection. Intraorally, the patient had exposed bone in the area of the previous tooth extraction with tissue inflammation and mild purulent drainage from the area. She had no fevers, chills, or significant trismus. A panoramic radiograph and Cone Beam Computed Tomogram (CBCT) scan were obtained at that office visit which showed osteolytic changes consistent with the diagnosis of osteomyelitis (Fig. 11.1a–c).

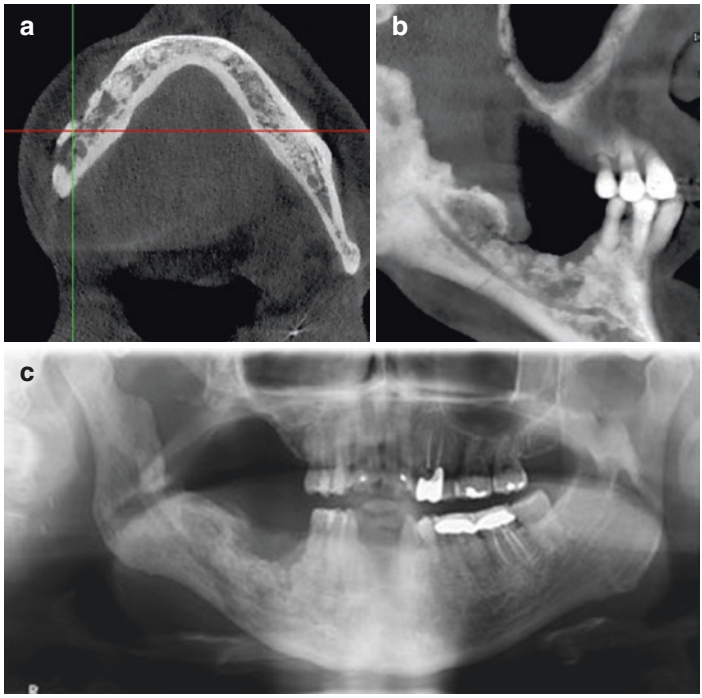


Figure 11.1 (**a**) Axial view of CT scan of the mandible demonstrating significant osteolytic change. (**b**) Sagittal view of the mandible on CT showing osteolytic changes in body region. (**c**) Panoramic radiograph showing osteolytic changes at superior border of body region

Approximately 1 week after the initial appointment, the patient was taken to the operating room for debridement and resection of the affected bone area, placement of an osseous reconstruction plate, and primary soft tissue closure. Intraoperative bone cultures were obtained which demonstrated necrotic bone with few mixed aerobic/anaerobic bacteria resembling mixed respiratory flora. A musculoskeletal infectious disease (ID) consult was obtained to help with the antibiotic coverage for the patient's chronic suppurative osteomyelitis, and a PICC line was placed on the day of surgery. She was discharged 2 days after surgery on ertapenem 1 gram daily intravenously via home health care.

The infectious disease service continued to follow the patient's CBC, ESR, CRP, and LFTs. She continued to be followed by OMFS as well, and 6 weeks postoperatively the patient was found to be pain-free with no purulent drainage or exposed mandibular bone. She was then given a 2-week course of PO Augmentin by the ID team and has not had any recurrence of symptoms to date. She continues to be followed by the OMFS team for possible secondary reconstructive bone grafting, likely an anterior iliac crest bone graft.

## Case #2: Secondarily Infected Chronic Fracture Mimicking Osteomyelitis

A 38-year-old female with a history of chronic hepatitis C, polysubstance abuse, and bronchitis presented to the emergency department (ED) with a complaint of intraoral drainage, left-sided facial swelling, as well as multiple mobile teeth. She presented with a temperature of 35.8 °C, stable vital signs, and no leukocytosis. Extraoral physical exam was significant for left submandibular fistula formation, left-sided submandibular swelling, and left-sided cranial nerve $V_3$ paresthesia. Intraoral physical exam revealed purulence coming from an area of exposed anterior mandibular alveolar bone, multiple mobile teeth, as well as a mobile left anterior mandibular segment. Panoramic radiograph and a CT scan of her

neck, with and without contrast, were obtained and demonstrated a left-sided mandibular parasymphysis pathologic fracture with adjacent osteolytic changes that appeared exactly as would be seen in typical osteomyelitis (Fig. 11.2a, b). In addition, it was noted that she had multiple grossly carious and severely periodontally involved teeth. She then reported being assaulted about 3 weeks prior but had never reported to the emergency department (ED) to be evaluated.

During the current ED visit, under local anesthesia, a 26-gauge wire was placed around multiple teeth on both sides of the fracture line and twisted in the midline (i.e., "a bridal wire") in order to minimize mobility of the two fractured mandibular segments. The patient was admitted to the internal medicine service to assist with the management of withdrawal symptoms, and she was started on 3.375 g of Zosyn intravenously every 6 hours. The patient was taken to the operating room 2 days after admission for debridement of her left mandibular parasymphysis followed by open reduction and internal fixation via an extraoral approach, closed reduction with maxillomandibular fixation, left submandibular fistulectomy, and removal of three grossly carious teeth (Fig. 11.3a, b). Surgical pathology for bone biopsy returned as necrotic bone with acute inflammatory infiltrate.

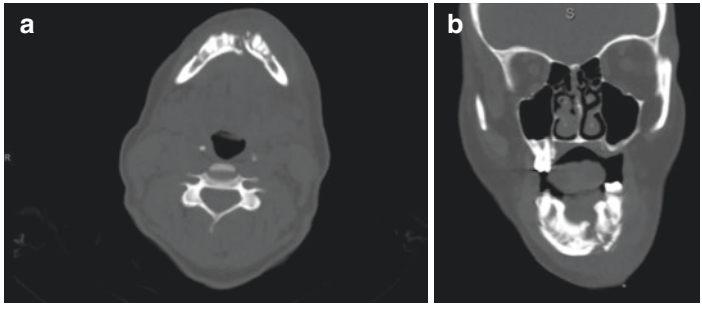


Figure 11.2 (**a**) Axial CT scan showing fracture of the mandible and adjacent osteolytic changes. (**b**) Coronal CT view showing fracture of the mandible and adjacent osteolytic changes

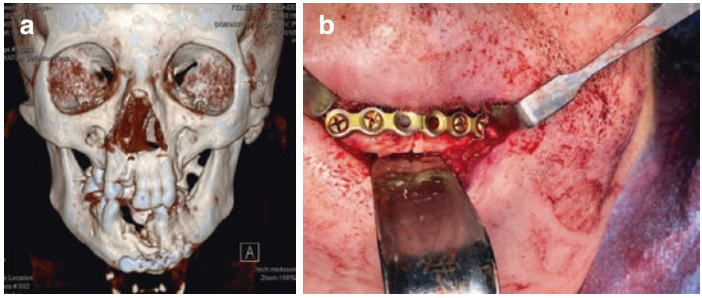


FIGURE 11.3 (**a**) 3-D reconstruction CT after debridement of necrotic bone and ORIF of fracture. (**b**) Intraoperative view of the mandible after debridement and ORIF

Cultures taken during surgery showed aerobic bacteria resembling mixed respiratory flora. The patient recovered well and was discharged later that day with a 2-week course of oral (PO) Augmentin. Although the medullary bone did demonstrate active infection from the displaced fracture segments, it is important to note that the OMFS team did NOT diagnose the patient with osteomyelitis due to no further osteolysis or progression of the infection other than the areas immediately adjacent to the fracture site. As such, it was not deemed necessary for the patient to undergo 6 weeks of IV antibiotics.

The patient followed up with the oral and maxillofacial surgery (OMFS) team, but before returning for her first follow-up visit at 1 week postoperatively, she had already cut her intraoral wires, releasing herself from maxillomandibular fixation. Although she had not been compliant with maxillomandibular fixation, she reported compliance with a soft non-chew diet. She reported to the OMFS clinic 1 month postoperatively with a mild degree of left mandibular swelling but no intraoral drainage. She was given an additional 2 weeks of PO Augmentin totaling 4 weeks of PO antibiotics and has since presented for her 2-month follow-up appointment with no signs of infection, drainage, or hardware failure.

## Discussion

Osteomyelitis of the maxillofacial region is distinguished from dentoalveolar abscesses or alveolar osteitis by inflammatory involvement of medullary bone and demonstrated evidence of continued osteolytic progression in areas adjacent to where the original infection began [1]. This is an important distinction. By definition, any infection from an odontogenic source, such as a "periapical lesion" (an infection that exits the root of a tooth and evidenced by a radiolucent area below the tooth), is already within the medullary bone of the mandible. This occurs thousands of times every day. Similarly, the simple presence of exposed oral bone is also not osteomyelitis. Every tooth extraction site will have bone exposed for up to a week or more, yet they heal quite well on their own with no intervention. Contrary to widespread misunderstanding in the infectious diseases community, these common infections and exposures within the mandible and maxilla are NOT osteomyelitis. This is in contradistinction to long-bone infections which represent an entirely different vascular picture. It is only when there is progression of this infection causing osteolytic changes throughout adjacent medullary bone within the mandible or maxilla that classifies the condition as osteomyelitis as demonstrated in Fig. 11.1a–c. Osteomyelitis of the facial bones is most common in the mandible largely due to its relatively poorer blood supply and greater bone density relative to the maxilla. Systemic factors such as an immunocompromised state, various chemotherapeutics, antiangiogenic medications, bisphosphonates, and radiation also can play a significant role in the development of osteomyelitis [1]. For the purpose of this text, the specifics of medication-related osteonecrosis of the jaw (MRONJ) or osteoradionecrosis (ORN) with superimposed infection will not be discussed as they are secondary, not primary, forms of bone infection [2, 3]. Osteolysis in these cases is due to the MRONJ or ORN, which then becomes *secondarily* infected and does not represent true osteomyelitis. In these cases, even in the absence of long-term antibiotics, the infection will usu-

ally be controlled with management of the underlying bone disease. The majority of true osteomyelitis that occurs in the mandible stems from an odontogenic source, such as after removal of teeth (as in the first case) or after root canal therapy by a dentist [1]. However, osteomyelitis of the mandible also may occur due to a fracture that has not undergone appropriate reduction and fixation [2]. In addition, many of these patients also present with other grossly carious dentition contributing to the infection due to the bacterial load. An untreated displaced fracture does not allow for adequate delivery of vascular supply from overlying periosteum and intramedullary systems. This may lead to an increase in neutrophils resulting in an increased intramedullary pressure ultimately leading to congestion of the vascular supply to surrounding bone and progression to osteomyelitis [2]. However, as seen in the second case, not all untreated displaced fractures that become secondarily infected are to be considered osteomyelitis. They must also present with extensive osteolytic change that extends beyond the area of the original infection, which in this case is the fracture site.

## Classifications and Clinical Presentations

There are multiple classification schemes for osteomyelitis, but the most widely accepted system separates osteomyelitis into acute and chronic, with chronic being defined as at least lasting 1 month [2]. The acute forms are as follows: contiguous focus, progressive and hematogenous. The chronic forms can be classified as recurrent multifocal, Garre's osteomyelitis, suppurative, nonsuppurative, and sclerosing [2, 3]. The main distinction to keep in mind from these classifications is acute vs. chronic and suppurative vs. nonsuppurative. Suppurative osteomyelitis is an infection of the medullary bone that produces purulence as opposed to sclerosing osteomyelitis which causes a thickening of the trabecular network from the endosteum without purulence production [4]. Many patients with acute suppurative osteomyelitis will present with fever, leukocytosis, trismus,

and possible paresthesia associated with compression of the inferior alveolar nerve [5]. Those with chronic suppurative osteomyelitis will more commonly present with evidence of an oro-cutaneous fistula. However, the findings that distinguish chronic versus acute forms are generalizations and great variability exists. This is highlighted in the cases above, where the patient who did not have a true osteomyelitis developed an oro-cutaneous fistula and the patient with chronic suppurative osteomyelitis did not [4]. Chronic sclerosing osteomyelitis characteristically produces severe pain that may increase or decrease, but some level of persistent pain will always remain. There may also be periods of mandible expansion and even associated soft tissue edema but no purulence production. Garre's osteomyelitis, also termed osteomyelitis with proliferative periostitis or periostitis ossificans, is a variant of chronic osteomyelitis where there is formation of new paracortical bone. It typically occurs in children due to their greater blood supply and increased bone regeneration capacity. The expansion of the bone associated with Garre's osteomyelitis is typically hard, not tender to palpation, and there is no associated purulence [6].

## Imaging

It is not uncommon for very early acute osteomyelitis to have a normal radiographic appearance [7]. A panoramic radiograph is obtained initially, often followed by CT with and without contrast, in order to evaluate any associated soft tissue infection that has occurred secondarily. The radiograph may demonstrate one or more smaller fragments of bone separate from the mandible or maxilla which are termed sequestra. The radiolucent area separating a bony fragment from the parent bone is termed an involucrum [8]. If osteomyelitis becomes very severe, approximating the inferior border of the mandible, it may result in a pathologic fracture. In chronic sclerosing osteomyelitis, the sclerotic nature on imaging may appear similar in appearance to various fibro-

osseous lesions, which should be included in the differential diagnosis (e.g., cemento-osseous dysplasia, fibrous dysplasia, etc.). Radiographically, Garre's osteomyelitis can mimic Ewing's sarcoma with the classic "onion skin" appearance that may be concerning for patients in this age range [6].

## Surgical and Antibiotic Management

Although there may be slight variations in treatment of osteomyelitis depending on its classification, the general principles for treatment of osteomyelitis are similar in that they require appropriate antibiotics combined with surgical management [1]. If possible, it is ideal to obtain a bone culture due to higher bacterial counts as compared with culture swab prior to initiation of antibiotic therapy. Unfortunately, much of the time, the anaerobic oral flora can pose a challenge to culture, oftentimes not yielding useful results. Classically, a 6-week course of IV antibiotics is required when considering chronic, refractory, or severe acute osteomyelitis [9–11] . However, if caught at an early stage or in low-grade chronic osteomyelitis, it has now been shown that certain cases may only require a short course of IV antibiotics followed by 4–8 weeks of oral antibiotics based on close clinical follow-up [10]. ESR and CRP, although nonspecific inflammatory markers, are useful to follow the progression of the disease and to tailor antibiotic duration. Many microorganisms such as *Prevotella*, *Porphyromonas*, *Staphylococcus*, and *Fusobacterium* species are resistant to penicillin. Because of this, beta-lactamase-resistant antibiotic coverage is ideal [9]. IV antibiotic options include, but are not limited to, ampicillin/sulbactam, piperacillin/tazobactam, meropenem, or ertapenem. These particular antibiotics are chosen due to their resistance to a variety of beta-lactamases in addition to their bactericidal activity against gram-positive and gram-negative aerobic and anaerobic bacteria [9]. The efficacy of this traditional treatment was demonstrated in case number one where the patient improved after the appropriate 6-week course of IV ertape-

nem. This is in contrast to case number two which did not demonstrate evidence of a true osteomyelitis and was amenable to a total of 4 weeks of oral Augmentin, also resulting in a positive outcome.

Historically, *S. aureus* and *S. epidermidis* were known to account for the majority of osteomyelitis of the maxilla and mandible, but recently this has decreased due to improved methods of identification. Currently, B-hemolytic strep and anaerobes such as those listed above are responsible for the majority of osteomyelitis of the jaws [11]. Chronic sclerosing osteomyelitis is typically caused by various *Actinomyces* species in mutualism with *Eikenella corrodens* in which penicillin-like antibiotics are the drug of choice [12].

Surgical treatment is based on the premise of removal of necrotic devascularized bone until bleeding bone is reached. Ideally, tight primary closure is obtained to allow the periosteum to lay adjacent to bone to further increase blood supply. Conservative debridement is typically the first-line treatment. If there is extensive osteomyelitis or a pathologic fracture occurs, treatment may ultimately require resection of the involved area and placement of an osseous reconstruction plate. This can then be followed by an additional surgery for secondary reconstruction with vascularized or non-vascularized bone graft [11]. It has been shown that secondary reconstruction with bone grafting must wait several months until the osteomyelitis has completely resolved. The exception to the classic debridement intervention is Garre's osteomyelitis. In this situation, removal of the offending source of infection, such as a dental extraction or root canal therapy of the necrotic tooth, followed by a 7–10-day course of empiric antibiotics is curative [6]. Another possible adjunct to treatment of osteomyelitis is hyperbaric oxygen (HBO) therapy which has been shown to increase the vascularity of the mandibular bone. This has been shown to aid in healing during treatment of osteomyelitis in select cases, especially in recurring disease, but does not guarantee improved results and may not be necessary in all cases [11]. Unfortunately, HBO therapy is often not feasible financially or geographically for all patients.

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# Chapter 12
# Flexor Tenosynovitis of the Hand

**Sandra B. Nelson and Alison C. Castle**

A 40-year-old male welder with a 20-pack-year smoking history and hypertension presents to the emergency department with acute pain and swelling involving his right thumb. Two days previously a piece of shrapnel pierced the pad of his thumb at work. The shrapnel was removed by the patient who then cleaned the area with soap and water and applied a topical antibiotic ointment. Despite these measures the area around the wound became progressively more swollen, erythematous, and painful. By the following day, the swelling engulfed his entire thumb. On presentation he denies any fevers or chills. He does not take any medications and he denies any allergies.

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J. Reznicek et al. (eds.), *Musculoskeletal Infections*,
https://doi.org/10.1007/978-3-030-41150-3_12

***Physical Exam*** Temperature 37.6° C; pulse 90; respirations 16; blood pressure 150/92. He is nontoxic appearing. Extremities: Right hand with diffuse, symmetrically swollen first digit with erythema. The thumb is slightly flexed at rest. Pain is elicited with passive extension of digit and with light palpation along the entire thumb. Area of puncture wound noted over proximal phalanx with scant non-purulent drainage.

***Laboratory Findings*** WBC 16,800/μl with 89% neutrophils, 1.2% bands, 8% lymphocytes. ESR 46 mm/hour, CRP 25 mg/L. Culture from wound base pending. Gram stain with gram-positive cocci in clusters. Plain films (Fig. 12.1) and MRI (Fig. 12.2) of the fourth digit: see below.

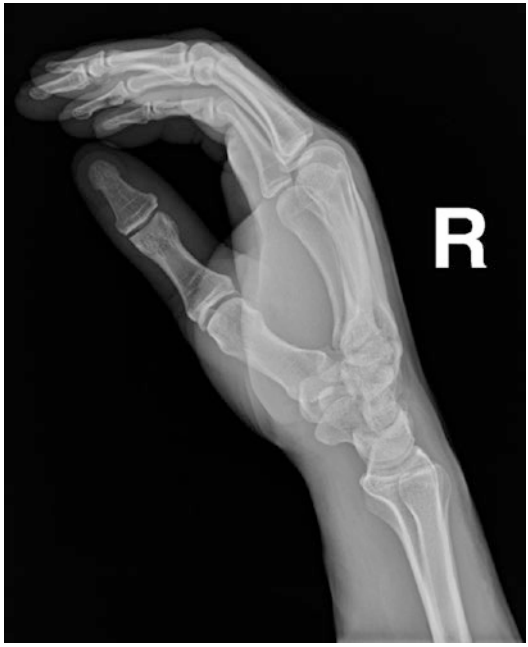


Figure 12.1 Plain film of the hand (lateral view) demonstrates no foreign body. Volar soft tissue swelling and loss of definition of fat planes in the wrist are also noted

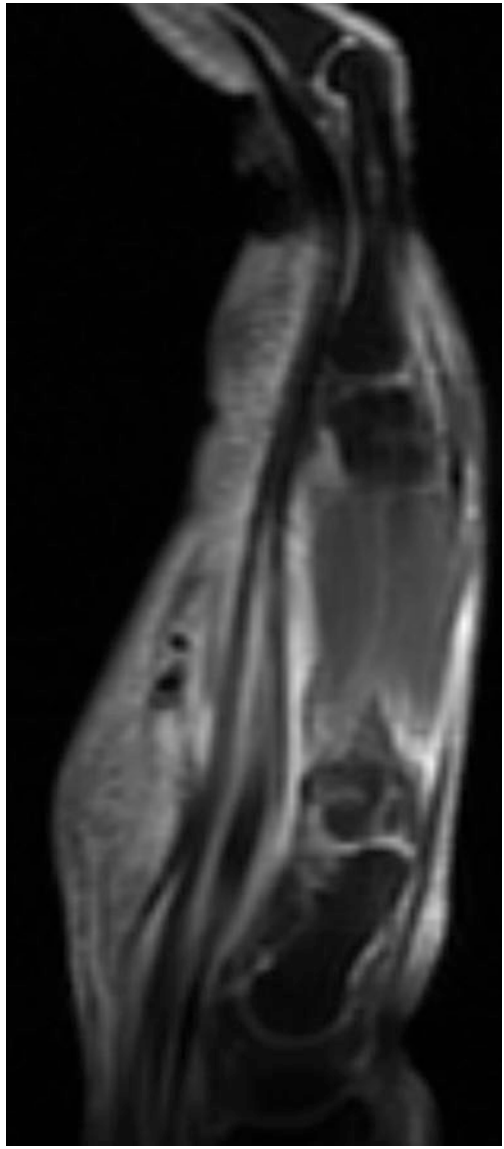

FIGURE 12.2 Sagittal MRI (T1 post-contrast with fat suppression) demonstrates fluid within the flexor pollicis longus tendon sheath as well as surrounding tissue edema and enhancement

## Question: What Is Your Diagnosis?

***Diagnosis*** Pyogenic Flexor Tenosynovitis

## Discussion

Pyogenic flexor tenosynovitis is an infection that occurs when bacteria are inoculated between the two sheaths that encapsulate tendons in the hand and wrist. The flexor tendon sheaths are comprised of an inner visceral layer and an outer parietal layer which join at the proximal and distal ends of the fingers to form a closed compartment. When organisms are introduced into this potential space, it fills with inflammatory cells and fluid, thus leading to the cardinal clinical features of tenosynovitis. Notably, extensor tenosynovitis on the dorsal surface of the hand is usually less severe than flexor tenosynovitis, as the extensor tendon sheaths are not fixed by a retinacular system; extensor synovitis may therefore be more difficult to distinguish from cellulitis.

Organisms may be introduced into the sheath compartment through puncture wounds, secondary to contiguous spread from adjacent infected soft tissue or occasionally via hematogenous spread. Hematogenous infection is characteristic of disseminated *Neisseria gonorrhoeae*, which favors the extensor tendons. Many organisms can cause infectious tenosynovitis; the most common are *Staphylococcus* and *Streptococcus* species. Depending on the nature of the exposure, organisms such as *Pasteurella multocida* (bite wounds), *Sporothrix schenckii* (penetrating rose thorn), other molds (environmental exposures), and *Mycobacterium marinum* (exposure to salt water or fish tanks) can be present. Monomicrobial infection is most common, though polymicrobial infection may occur, particularly in the setting of bite wounds.

The clinical presentation of flexor tenosynovitis was first described by Allen Kanavel in 1912. The four Kanavel signs are significant pain with passive extension of the

digit, symmetric or fusiform enlargement of the affected digit, digit maintained in flexed position at rest, and tenderness along the course of the flexor tendon sheath [1]. The presence of any of these signs following a puncture wound should raise suspicion of possible flexor tenosynovitis. Flexor tenosynovitis can be staged according to preoperative findings; most patients present in disease stage I or II which includes an inflamed sheath manifested by Kanavel signs with or without subcutaneous purulence (Table 12.1). Patients in stage III have evidence of digital ischemia and fare poorly due to septic necrosis and destruction of the tendon sheath [2, 3].

Smokers are more likely to present with an advanced stage on presentation and have delayed wound healing after intervention [4]. Immunosuppressed patients, such as those with diabetes, human immunodeficiency virus (HIV) infection, malignancy, or long-term corticosteroid therapy, are more likely to have polymicrobial or slow-growing organisms [4].

The diagnosis is usually made clinically; however imaging studies such as plain film radiographs and MRI can support the clinical impression, evaluate for the presence of foreign body, and assist with understanding the extent of surgical debridement needed. The differential for tenosynovitis includes herpetic whitlow, septic arthritis, crystal-induced arthritis, paronychia, felon, cellulitis, and other deep space infections of the hand, such as a "horseshoe abscess." One

Table 12.1 Progression of acute flexor tenosynovitis

| Stage | Clinical features | Intervention |
|---|---|---|
| I | Distention of sheath with exudative fluid | Irrigation and drainage |
| II | Distention with purulent fluid, invasion into subcutaneous areas | May require partial or complete tenosynovectomy |
| III | Septic necrosis with involvement of the tendon | Debridement of sheath and necrotic tissue<br>Possible amputation |

distinguishing feature of paronychia and felons includes palpable fluctuance or tense localized swelling as opposed to the diffuse symmetric swelling seen with flexor tenosynovitis.

To assist with microbiologic diagnosis, purulent drainage may be cultured for bacterial pathogens. If there is no drainage to culture, appropriate samples are commonly obtained at the time of surgical debridement. In subacute and indolent infections, the diagnosis may not be as obvious and the need for surgery not urgent. In these cases percutaneous sampling of the tendon sheath and/or fluid may be considered to facilitate diagnosis. In the setting of subacute onset, fungal and mycobacterial cultures should be obtained in addition to bacterial cultures, particularly in the right epidemiologic context.

The gold standard for treatment of acute bacterial flexor tenosynovitis includes prompt initiation of intravenous antibiotics and urgent surgical debridement. Initial broad-spectrum antibiotics should target common pathogens; a typical regimen may include vancomycin and a third-generation cephalosporin. The regimen is then tailored once the organism, or organisms, are identified and sensitivities known. Surgical consultation should be made as soon as clinical suspicion exists in order to expedite operative drainage and debridement of the involved digits and/or hand. The limb may also be elevated with protective splinting, activity restricted, and anti-inflammatory medications administered. Stage I infections may be managed with irrigation of the tendon sheath alone; however stages II and III require tendon debridement. Long-term complications of flexor tenosynovitis include finger stiffness, tendon sheath adhesions, tendon necrosis, and amputation [3]. Although rare, there have been studies demonstrating successful management of acute pyogenic flexor tenosynovitis with intravenous antibiotics alone and close clinical monitoring, but further larger prospective studies are needed to assess outcomes [5].

This patient received broad-spectrum antibiotics and was taken immediately for surgical debridement. He was found to have purulence within the tendon sheath, but no evidence of

spread to other bursal structures or soft tissue abscess. Preoperative and operative cultures grew methicillin-sensitive *Staphylococcus aureus* and his antibiotics were de-escalated to cephalexin. After treatment for infection, he ultimately recovered normal digit function.

**Clinical Pearls**

1. Pyogenic flexor tenosynovitis is an infection that develops between the parietal and visceral flexor tendon sheaths of the digits; severe forms may result in long-term morbidity.
2. The four classic Kanavel signs include pain with passive extension of the digit, symmetric or fusiform swelling, flexed finger at rest, and tenderness to palpation along the course of the tendon sheath. Plain radiographs and MRI can help rule out bone involvement and foreign body.
3. Empiric treatment involves broad-spectrum antibiotics that may be tailored once an organism is known. The clinician should be aware of exposures that may lead to unusual organisms.
4. Early surgical irrigation and/or debridement is considered essential for functional recovery.

**Acknowledgment** The authors would like to acknowledge F. Joseph Simeone, M.D., for assistance with image preparation.

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# Chapter 13
# Acute Paronychia and Felon

**Glenn E. Lee and Jonathan Isaacs**

## Case 1: Acute Paronychia

A 26-year-old female nurse presents with 4 days of worsening swelling and pain of her nondominant left ring finger. She denies trauma or nail biting. On examination, she has erythema, fluctuance, and tenderness of the eponychium as well as the paronychium of the ulnar aspect of her left ring finger (Fig. 13.1). There is no active drainage. There is no tenderness of the volar pulp of her finger or along the flexor tendon sheath. She has full and painless range of motion of her DIP and PIP joints. Radiographs show soft tissue swelling dorsally, but are otherwise negative.

## Case 2: Acute Felon

A 59-year-old male with type 2 diabetes mellitus presents with 6 days of progressively worsening throbbing pain and swelling of the pulp of his nondominant left index finger. He reports that he removed a splinter from that area a week ago.

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J. Reznicek et al. (eds.), *Musculoskeletal Infections*,
https://doi.org/10.1007/978-3-030-41150-3_13

Figure 13.1 Acute paronychia of the left ring finger. (Courtesy of Maria Slobodnik)

On examination, he has exquisite tenderness of the pulp of the affected digit. There is a fluctuant area with visible subcutaneous purulence and surrounding erythema (Fig. 13.2). It does not extend past the flexion crease of the DIP joint. There is no tenderness along the flexor tendon sheath and he has painless range of motion of the DIP joint. Radiographs show soft tissue swelling of the pulp but there is no foreign body and there are no signs of osteomyelitis.

## Discussion

### *Evaluation*

Acute paronychia is a soft tissue infection of the nailfold and is diagnosed clinically. It initially presents with tenderness, swelling, and erythema of the paronychium and/or the eponychium and often progresses to an abscess (Figs. 13.3 and 13.4). Purulence may track underneath the nailplate which may cause injury to the germinal matrix or to the pulp of the digit leading to a felon. Risk factors for acute paronychia include minor trauma, onychophagia, hangnails, and manicures [1].

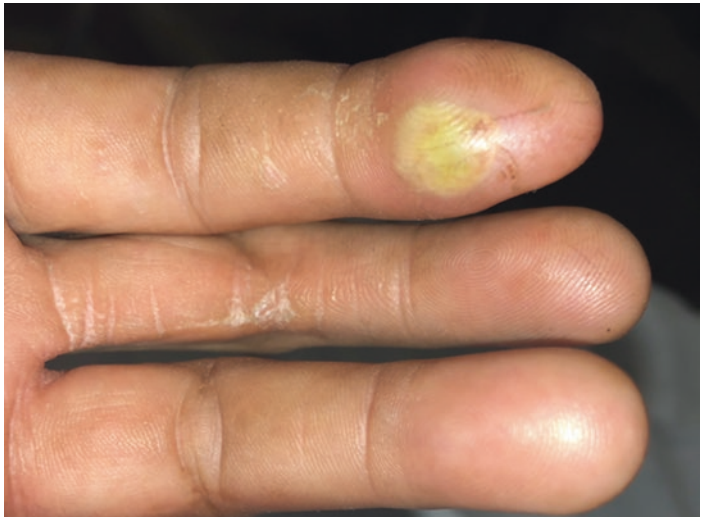

FIGURE 13.2 Acute felon of the left index finger. (Courtesy of Mackenzie Grasso, MD)

Acute felon is a soft tissue infection of the pulp or the volar pad of the digit and is diagnosed clinically as well. Patients typically present with progressively worsening throbbing pain, tenderness, and swelling. Felons are frequently a result of penetrating trauma [1]. Diabetics can develop felons from fingerstick blood glucose checks. The anatomy of the pulp of the digit is unique in that it is formed by a network of septal compartments. These septa connect the epidermis to the periosteum of the distal phalanges in order to stabilize the soft tissue during pinch and grasp. Increased pressure from an enlarging abscess and associated soft tissue inflammation can lead to microvascular compromise and cause tissue necrosis due to the non-distensible nature of these septa (Fig. 13.5). Additionally, the pressure can cause necrosis of the periosteum and resultant osteomyelitis of the distal phalanx [2].

When evaluating a patient with fingertip infections, proximal aspects of the digit on both the volar and dorsal surfaces

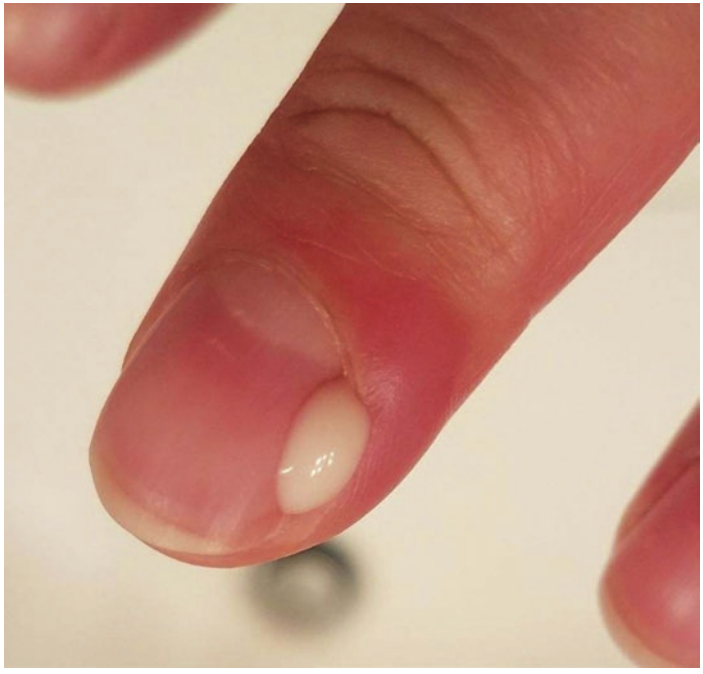

Figure 13.3 Acute paronychia with abscess formation. (Courtesy of Julie Reznicek, DO)

should be assessed for erythema, tenderness, and swelling as not to miss concomitant infections such as pyogenic flexor tenosynovitis or septic arthritis. Laboratory workup is often unnecessary unless the patient is having symptoms or signs consistent with systemic illness. Radiographic evaluation may be helpful, especially in subacute cases, to rule out osteomyelitis.

## *Management*

Early acute paronychia and felon prior to the formation of an abscess can be treated conservatively with oral anti-staphylococcal antibiotics [3–5]. Warm soaking is often rec-

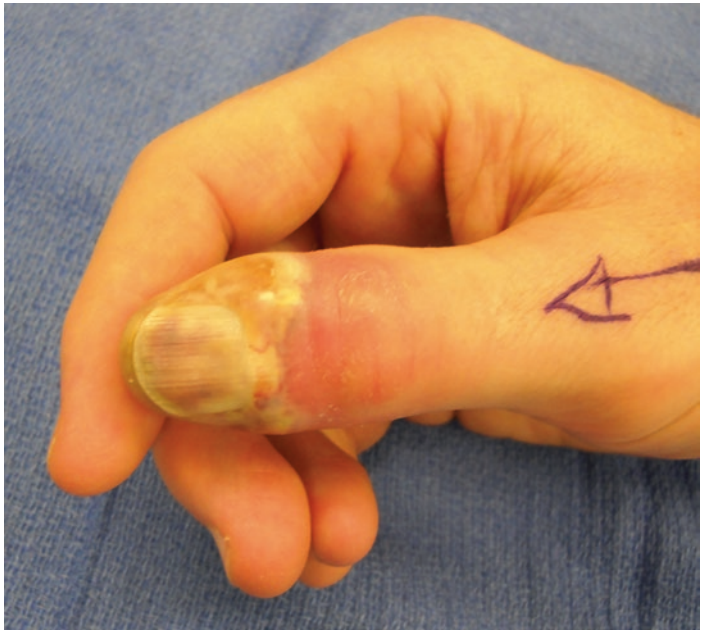

FIGURE 13.4 Acute paronychia with abscess formation. (Courtesy of Warren Hammert, MD)

ommended in the literature but there is no high-level evidence to support its efficacy [4]. Patients usually present after development of an abscess, which requires irrigation and debridement (I&D). This can be performed in the clinic or emergency room setting. There are no studies comparing outcomes for different techniques of I&D, so we provide our preferred methods for decompression.

In both paronychia and felon, the affected digit is anesthetized with a digital block with lidocaine. A finger tourniquet is applied to the base of the digit to provide a relatively bloodless field. The digit is prepped and draped in sterile fashion.

For paronychia, a longitudinal incision is made extending proximally from the junction of the eponychium and paronychium (Fig. 13.6). A small hemostat or dissection scissors

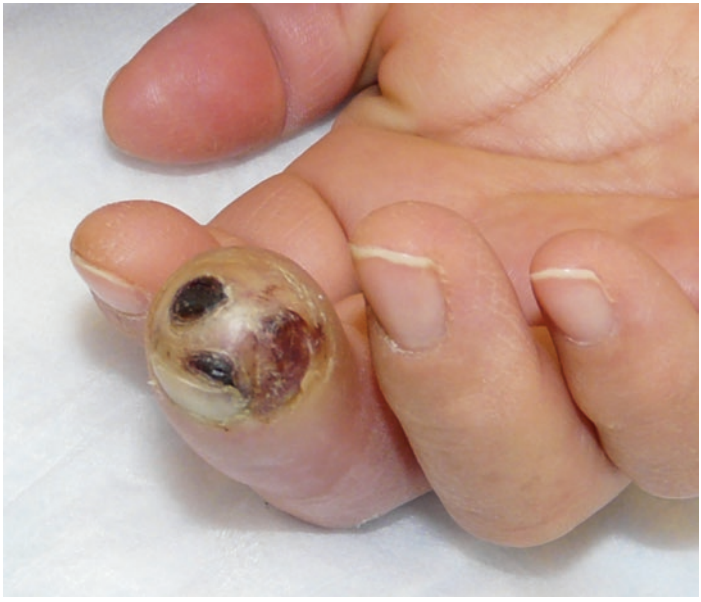

Figure 13.5 Acute felon with microvascular compromise and tissue necrosis

are used to bluntly decompress the abscess around the nailfold. If purulence tracks down underneath the nailplate, a part of the nailplate or the entire nailplate should be removed. If there is a concern for felon, a separate incision will facilitate blunt dissection which should be carried along the distal phalanx into the pulp of the digit. The septa of the pulp should be released with sharp dissection as further described below.

Many different techniques have been described for I&D of a felon. Our preferred approach is a high lateral incision extending longitudinally from the pulp to the flexion crease of the DIP joint (Fig. 13.7). The incision should be placed just volar to the lateral nailfold to avoid iatrogenic neurovascular injury. We recommend placement radially for the thumb and small finger and ulnarly for the other three digits. This avoids the formation of a tender scar along areas that are frequently

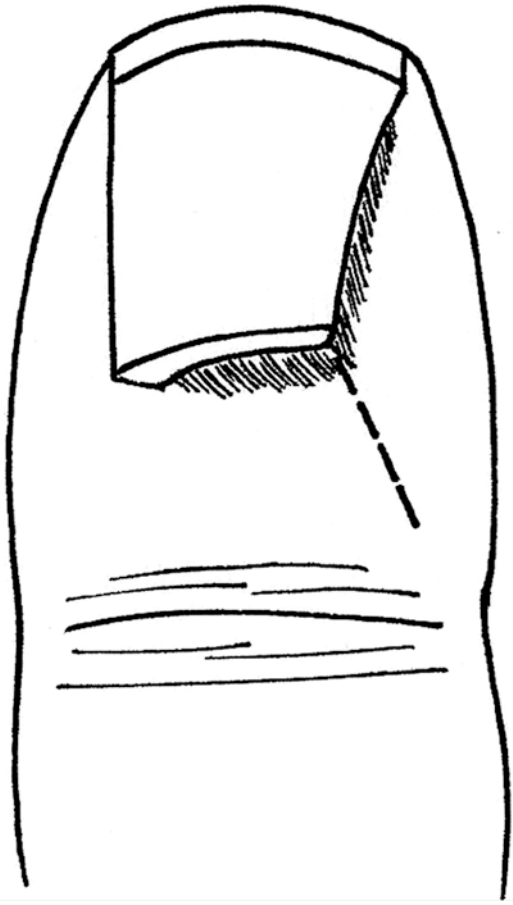

Figure 13.6 Decompression of an acute paronychia, via a longitudinal incision extending proximally from the junction of the eponychium and paronychium

used for pinch [3]. It is imperative to break up or release all of the septa in order to adequately decompress the many microabscesses within the pulp. Dissection into the flexor sheath should be avoided. The volar cortex of the distal phalanx can be probed to assess for softening of the bone sugges-

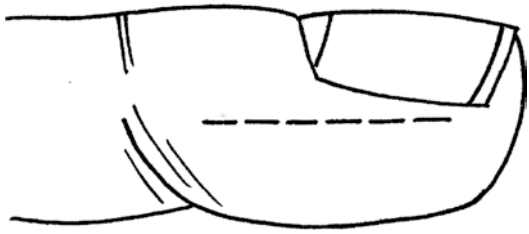

FIGURE 13.7 Decompression of an acute felon, via a high lateral incision extending longitudinally from the pulp to the flexion crease of the DIP joint

tive of osteomyelitis. Osteomyelitis may require more extensive debridement or even amputation to adequately treat the infection.

Wound cultures should be taken during the debridement procedure to guide antibiotic therapy. The most common organisms that cause paronychia are *Staphylococcus aureus*, *Streptococcus pyogenes*, *Pseudomonas pyocyanea*, and *Proteus vulgaris* [1, 4]. Polymicrobial cultures are common [6]. Felons, on the other hand, are most commonly caused by *Staphylococcus aureus* [1, 3, 5]. Historically, cephalexin and amoxicillin-clavulanate have been acceptable first-line oral agents for these infections. However, there has been an increasing incidence of hand infections from community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) [7–10]. Imahara et al. performed a single-center retrospective review of hand infections during a 10-year period. Incidence of CA-MRSA hand infections rose 41% each subsequent year compared to non-MRSA infections [11]. Prospective case series by Pierrart et al. and Rabarin et al. demonstrated resolution of all fingertip infections without post-procedural administration of antibiotics. However only two patients in Pierrart's study and no patients in Rabarin's study had cultures positive for MRSA. Thus, the local prevalence of MRSA should be considered to avoid improper initial antibiotic selection [12, 13]. The Centers for Disease Control currently recommends empiric MRSA cov-

erage if local prevalence exceeds 10% [7]. Risk factors for CA-MRSA infection include intravenous drug usage, immunosuppression (i.e., diabetes mellitus, HIV), incarceration, and history of prior MRSA infection [11, 14]. However, an increasing trend of CA-MRSA hand infections has been documented even in patients without risk factors [10]. Sulfamethoxazole-trimethoprim covers most isolates of CA-MRSA. Clindamycin and ciprofloxacin may appropriately treat some isolates, but up to 50% of infections exhibit regional resistance [1, 7].

Special consideration regarding antibiotic regimen should be given to fingertip infections caused by oral flora. The most common species isolated from infections caused by human oral flora are *Staphylococcus aureus*, beta-hemolytic *Streptococci*, and *Eikenella corrodens*. Similar to human bite wound infections, the combination of amoxicillin-clavulanate and clindamycin is usually sufficient empiric therapy for paronychia caused by nail biting. If the patient is penicillin allergic, alternative agents include doxycycline, sulfamethoxazole-trimethoprim, or clindamycin plus a fluoroquinolone [1, 3, 14].

In all cases, cultures should be followed and antibiotics tailored to speciation and specificities. Outpatient treatment is usually successful for uncomplicated cases. However, admission for intravenous antibiotics may be necessary for severe or refractory cases and in patients with systemic symptoms [7].

Daily "wet-to-dry" gauze packing is frequently recommended in the literature following I&D, but there is no high-level evidence to support its use [4]. However, we do regularly instruct our patients to perform packing changes for several days in order to facilitate continued drainage of the abscess as there are no significant risks other than patient discomfort. We have seen recurrent infections in patients that do not follow this regimen. Some authors recommend iodine soaks following I&D, but a randomized trial by Tosti et al. demonstrated that it does not lead to better outcomes in acute hand infections when compared to dressing changes alone [15].

Some providers utilize whirlpool therapy, but again, this adjuvant therapy lacks high-quality evidence to suggest that it successfully removes debris or reduces bacterial bioburden [16]. Whirlpool therapy also portends the potential risk of delayed wound healing via disruption of granulation tissue and hindrance of migrating epidermal cells [17]. Furthermore, whirlpool therapy can lead to wound maceration, and there have been reports of *Pseudomonas aeruginosa* infections from contaminated hydrotherapy equipment.

Patients should be followed closely for resolution of symptoms and wound healing. Repeat debridement and admission for intravenous antibiotics may be required if improvement is not seen after 4 or 5 days. Patients with comorbid conditions may require a longer period of time for recovery. Hypersensitivity from healed surgical scars can persist for several months or sometimes indefinitely. Nailplate deformities can occur after paronychia either from the infection or iatrogenic injury to the germinal matrix [18]. Permanent pulp atrophy can occur even after successful treatment of felon. Pulp instability from the disruption of septa is an uncommon complaint but may take up a year to resolve [2]. Finally, the neurovascular structures are at risk from malpositioned incisions or overaggressive dissection.

## *Differential Diagnosis*

Important conditions to consider in the differential diagnosis of fingertip infections are chronic paronychia and herpetic whitlow. Chronic paronychia is a distinct process from acute paronychia and not merely a long-standing form of it. It is caused by excessive exposure to moisture and is most common among dishwashers, bartenders, swimmers, and medical professionals. Intermittent episodes of eponychial inflammation and drainage lead to nailfold separation from the nailplate and resultant infection. Causative organisms include bacterial species, atypical mycobacteria, and fungi [1, 14]. Treatment is often challenging and is outside the scope of this review. Herpetic whitlow is a fingertip infection caused by

herpes simplex virus. It is characterized by painful vesicles filled with clear fluid. Patients may present with viral prodromal symptoms. Diagnosis is clinical but can be confirmed with a Tzanck smear or viral cultures. The lesions usually heal without treatment in 3 weeks, undergoing a process of coalescence, drainage, ulceration, and resolution. Unnecessary debridement of herpetic whitlow may lead to bacterial superinfection. The virus enters latency following resolution and recurrence rate is around 20% [1, 3, 14].

**Follow-Up** Patients in both cases 1 and 2 underwent bedside irrigation and debridement. They were prescribed empiric sulfamethoxazole-trimethoprim. Both wounds healed uneventfully.

**Clinical Pearls**

1. Paronychia and felon prior to abscess formation can be treated with antibiotics alone.
2. Irrigation and debridement is the mainstay of treatment for fingertip abscesses.
3. There is an increasing rate of CA-MRSA hand infections. Local MRSA prevalence should be considered for antibiotic selection.
4. Antibiotics should cover oral flora for paronychia caused by nail biting.
5. Wet-to-dry gauze packing may decrease abscess reformation.

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# Chapter 14
# Hip Septic Arthritis in a Pediatric Patient

**Joanna J. Horstmann**

## Case

The patient is a 10-year-old female who is a healthy child. She presented to the emergency room after 2 days of left thigh and flank pain with difficulty walking. She had a fall about 4 days ago but did not injure her leg and was able to bear weight on it immediately after the injury. She woke up in the middle of the night with significant pain and fever. She did not have a history of any previous infections or viral illnesses in recent weeks.

On physical examination, the patient was very anxious and in obvious distress. There were no significant skin findings around her left hip or flank: no skin rashes or erythema identified. She had anguishing pain when attempting a slight logroll motion of her left hip. She was unable to stand up to ambulate.

Vital signs showed she met SIRS criteria with elevated heart rate, respiratory rate and temperature:

- BP 138/78, HR 134, RR 20, temperature 38.9 °C

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J. Reznicek et al. (eds.), *Musculoskeletal Infections*,
https://doi.org/10.1007/978-3-030-41150-3_14

Pertinent laboratory values:

- White blood cell count (WBC) 17.5
- CRP 23.1
- ESR 80
- Platelets 221
- Hemoglobin 13.1
- INR 1.5

Radiographs of the pelvis were obtained (Fig. 14.1). There was no gas throughout the soft tissues. There were no fractures of the proximal femur. There was no widening of the hip joint noted.

MRI of the pelvis was done urgently at patient presentation due to high concern of intrapelvic infection. This showed an effusion in the left hip with signal increase in the acetabulum concerning for osteomyelitis as well as surrounding edema in muscles around the hip consistent with myositis (Fig. 14.2).

A hip joint aspiration was performed upon completion of the MRI with results showing total nucleated count of 65,000 WBCs with 95% PMNs. The arthrocentesis did not show any crystals and the fluid was thick and turbid.

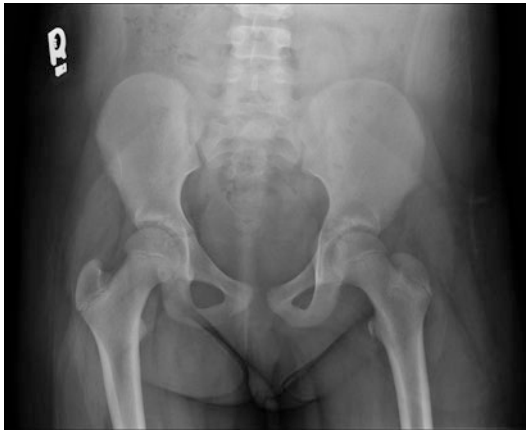

Figure 14.1 AP pelvis radiograph of patient presenting with a septic hip. Radiographic findings suggestive of effusion, but no other abnormalities seen. X-rays can appear normal with acute infection

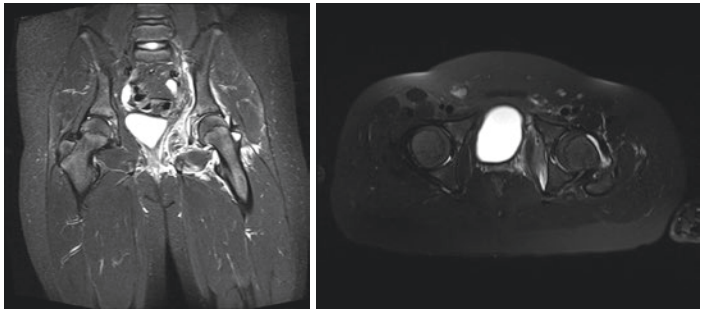

Figure 14.2 Coronal and axial slices of magnetic resonance imaging (MRI) of patient with complicated septic arthritis of left hip with surrounding myositis as well as increased signal in bony acetabulum concerning for osteomyelitis

Based on the patient's clinical presentation including history, physical examination, laboratory results and imaging findings, the patient was diagnosed with acute hematogenous septic arthritis of the left hip and taken emergently to the operating room. There, an open arthrotomy was made to the left hip using an anterior approach and purulent fluid was found upon entering the capsule of the hip joint. Cultures obtained from the joint fluid as well as capsule tissue were sent, resulting in the diagnosis of methicillin-resistant *Staph. aureus* (MRSA) infection. The patient was also found to have bacteremia with the same organism; however these results were not available for another 24 hours. The patient was started on empiric antibiotics immediately after surgery which were then transitioned to more specific treatment based on culture results and sensitivities. Once her bacteremia cleared, she was able to receive a peripheral (PICC) line in order to complete antibiotic treatment. While hospitalized, patient also developed a postoperative fever and increased work of breathing on day 3 after surgery. Further workup of her condition by computed tomography (CT) revealed the presence of a small pulmonary embolism that required treatment with anticoagulation. Following the successful treatment of both her infection and pulmonary embolism, the

patient was discharged home in 10 days and was able to return to full activities 3 months after surgery. She was followed closely for 2 years and, fortunately, did not appear to develop any long-term sequelae from her infection such as avascular necrosis, growth arrest or arthritic changes.

## Background

Pediatric septic hip arthritis is a rare but potentially devastating condition. It can occur at any age; however certain populations are at higher risk than normal. This includes preterm infants, patients with immunodeficiency, as well as patients with sickle cell disease [1].

## Pathophysiology

Pediatric hip joint infections typically occur due to hematologic spread. The hip joint is deep within the body and well protected from direct inoculation with bacteria due to minimal trauma. However, the majority of the blood supply arrives to the epiphysis of the joint (femoral head) through the physis in a complex blood supply network. Since the femoral head is intra-articular, blood carrying bacteria to the femoral head can easily be found in the joint, therefore causing infection.

Bacteria found in the joint capsule causes an inflammatory reaction activated by cytokines which, in addition to the body fighting the infectious organism, can also have deleterious effects on its own cartilage causing breakdown of proteins. These inflammatory changes can then cause long-term sequelae such as arthritis in the involved joint [1].

## Clinical Presentation

Symptoms of septic hip arthritis in children are numerous but can vary significantly with age. Infants can often be found to be inconsolable with decreased activity or appetite. Toddlers

may present with refusal to bear weight or decreased energy. Older children may present with groin pain, thigh pain, limping or pain with movement of the joint. All ages can have an associated fever with the condition, often >38 °C, irritability, and fatigue. Often, there has been a recent history of a viral infection such as an upper respiratory virus or gastrointestinal virus causing illness, fever, or rash. Patients can also have a history of a recent bacterial infection such as otitis media or a urinary tract infection. Onset of this condition is fairly sudden and typically worsens very quickly in 24–48 hours if not recognized and treated [1].

## Diagnosis

Clinical presentation along with laboratory studies can help providers make the diagnosis of septic hip arthritis. Such evaluations should happen swiftly; therefore obtaining multiple studies at a facility that is unable to provide definitive treatment is futile. Children should be examined clinically and patients with a strong suspicion of septic hip arthritis should be transferred immediately.

In addition to physical exam findings, laboratory studies are helpful in the diagnosis of septic hip arthritis. Due to this being a hematogenous process, systemic inflammatory markers are frequently elevated. White blood cell count, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) are obtained and are helpful in diagnosis and distinguishing septic arthritis from transient synovitis [2–6]. Blood cultures should be drawn immediately upon arrival, and if the child appears systemically ill or shows clinical signs of sepsis at presentation (elevated HR, elevated RR, fever), then antibiotics should be started. However, if not systemically ill antibiotics should be held until joint fluid studies are obtained for culture as this will guide future antibiotic treatment.

Kocher criteria were developed to help stratify the risk of having septic hip arthritis in children based on the following categories: (1) presence of fever, (2) inability to bear weight,

(3) WBC count of >12,000, and (4) ESR of >40. Having all four criteria present corresponds to nearly 99% chance of presence of septic arthritis of the hip and should require urgent evaluation/treatment [2–4, 6]. Children with only one criterion met are at lower risk but should still be monitored closely for clinical improvement.

Once a patient is identified as high risk, meeting all four criteria as above, further evaluation with imaging should be obtained. An ultrasound study is a very quick, inexpensive, and radiation-free way to evaluate the hip for the presence of an effusion and can be used as an adjunct when performing an aspiration of the joint. A sterile spinal needle can be placed into the hip with ultrasound guidance, and fluid can be aspirated in order to perform a fluid analysis, typically white blood cell count and differentiation. Fluids with >50,000 WBC and >90% PMNs are considered indicative of acute joint infection [7, 8]. Ultrasound can also be helpful in redirecting our differential diagnosis, especially in the absence of effusion as this may be more likely associated with osteomyelitis or pelvis abscess or in the presence of bilateral hip effusions, which is very unlikely to be septic arthritis but in most cases associated with transient synovitis or reactive arthritis that is typically due to viral illness [7, 8].

Most cases of pediatric septic hip can be diagnosed without additional advanced imaging. However, in cases of older children or patients with delayed presentation, magnetic resonance imaging (MRI) can be very useful in making the correct diagnosis as well as identifying additional findings such as the presence of osteomyelitis or intra-pelvis abscesses, both of which can mimic the presentation of a septic hip joint [8].

## Classification

Similar to other musculoskeletal infections, septic hip arthritis is categorized by the infectious organism involved. There are many possible pathogens, with *Staph. aureus* being the most common culprit.

Simple or uncomplicated septic arthritis is one that is recognized quickly, and the infection has not yet spread past the capsule of the joint. In complex septic arthritis, the infection has progressed beyond the involved joint and can also be found in surrounding muscle (myositis) and bone (osteomyelitis) [1, 9].

## Treatment

Treatment of septic arthritis of the hip requires a combination of surgical and medical management. Upon identification of the diagnosis, the hip joint in question should be drained. This is typically performed with an open arthrotomy using an anterior approach. This allows access to the capsule as well as visualization of the femoral head cartilage, meanwhile protecting blood supply to the femoral head which can be injured from a posterior approach [1, 9].

In addition to surgical treatment, antibiotics are a key component to successful treatment of the septic hip. Since joint and blood cultures are not always successful it is very important to identify the patient population and consider the most common bacteria found in that group. Empiric antibiotics can also differ based on patient factors. Patients at high risk for specific infections are neonates, who have a tendency to develop Group B streptococcal infections, and patients with sickle cell anemia, who are more likely to have *Salmonella* infections. Most pediatric joint infections are caused by gram-positive organisms including *Staphylococcus aureus* (MSSA and MRSA) [1, 9].

Empiric antibiotic treatment typically begins with gram-positive coverage using vancomycin and gram-negative coverage by using a third-generation cephalosporin such as ceftriaxone. Susceptibilities should be obtained on all cultured organisms in order to be most specific and streamlined with antibiotic choice. Uncomplicated pediatric septic hip infections are treated with a short-term course of intravenous antibiotics, typically about 2 weeks. Cases with complications, such

as late diagnosis, immunodeficient host, or bone involvement, may need up to 6 weeks of treatment [1, 9, 10]. This requires placement of peripheral intravenous access (PICC line) for home antibiotics. Prior to placing a long-term intravenous line, one must ensure that the patient has cleared all bacteremia, and if initial blood cultures are positive, these should be repeated until negative prior to placing long-term access.

Progress of treatment should be monitored using the same inflammatory markers obtained at diagnosis. WBC, ESR, and CRP will typically rise immediately after surgery, but WBC and CRP should improve greatly with appropriate treatment, often down 50% of their original values in 48–72 hours [1, 9, 10]. ESR is typically slower to improve and may take weeks to normalize.

Once a patient has completed their intravenous antibiotic treatment they are followed clinically for signs of complications or sequelae of their septic joint.

## Sequela

Prior to the use of intravenous antibiotic therapy, patients with septic joint arthritis frequently developed sepsis which leads to systemic multi-organ failure and ultimately death.

Fortunately, the ability to quickly and correctly diagnose the patient and emergent treatment with surgery and antibiotics have helped to minimize this grave complication. However, other long-term sequelae still do exist and result in difficult problems to manage long term in these otherwise healthy children.

Most worrisome complications of septic joint arthritis include avascular necrosis, growth arrest causing deformity, hip dysplasia or dislocation and development of postinfectious arthritis [11]. Their effects can range from minimal, giving the patient near-normal function of the hip, to catastrophic, where function is severely affected, altering gait mechanics, causing pain, joint destruction and inability to return to normal physical activities.

**Clinical Pearls**

1. Pediatric septic arthritis of the hip is a common condition that necessitates prompt diagnosis and treatment in order to avoid long-term complications.
2. Common clinical findings are children with fever, limp or difficulty walking, or even refusal to bear weight all together. Children are commonly laying down and holding their hip in a protected position of hip flexion and external rotation.
3. Laboratory studies help make this diagnosis, and use of Kocher criteria is recommended to identify patients at high risk: WBC > 12, ESR > 40, presence of fever >38 °C and inability to bear weight. CRP is also a useful marker and values >4 are concerning for presence of acute infection.
4. Radiographs are not very informative at making the diagnosis; however, ultrasound can be used to identify the presence of joint effusion – which can then be aspirated to evaluate the joint fluid.
5. Advanced imaging such as MRI should be used in cases of older children. This may not be available at all centers and should not delay care if not immediately available. MRI is helpful however in identifying surrounding myositis, osteomyelitis and subperiosteal abscess that may be the primary diagnosis or may coexist with a joint infection.
6. Treatment of septic arthritis involves drainage of the infection requiring a surgical approach in combination with bacterial-specific antibiotics once an organism is identified.
7. Long-term sequelae of pediatric hip joint infections can include hip dysplasia and dislocation, growth arrest causing deformity, avascular necrosis, arthritic changes, and fracture due to weakening of surrounding bone.

8. MRSA infections in particular are at higher risk of having combined joint and bone infections, higher risk of fracture through the infected area, as well as development of septic emboli that can cause a deep vein thrombosis (DVT) or pulmonary embolism (PE).

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# Chapter 15
# Chronic Recurrent Multifocal Osteomyelitis

**Emily Godbout and William Koch**

## Case

A 7-year-old female with no past medical history presented with bilateral hip pain, right greater than left, and fever. Laboratory evaluation revealed a normal white blood cell count, a C-reactive protein (CRP) of 2.06 mg/dL, and an erythrocyte sedimentation rate (ESR) of 63 mm/hour. Magnetic resonance imaging (MRI) was consistent with multifocal areas of bone edema and increased uptake in the right superior pubic ramus and the left femoral head involving the epiphysis, the femoral neck, and the greater trochanter. There was no drainable abscess noted. She underwent bone biopsy with findings consistent with chronic osteomyelitis, and cultures were negative for a microorganism. Antibiotics were not started. She improved on a short course of a nonsteroidal anti-inflammatory drug (NSAID). Over the next 4 years, she continued to have intermittent episodes of right-sided hip pain that improved with short courses of NSAIDs managed by a pediatric rheumatologist. At age 11, she had an episode

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J. Reznicek et al. (eds.), *Musculoskeletal Infections*,
https://doi.org/10.1007/978-3-030-41150-3_15

of increased pain in her right hip that was not relieved by NSAIDs. She remained afebrile. A repeat MRI revealed a persisting area of abnormality on the pelvic ramus. She underwent a second bone biopsy, which was negative for a microorganism. No antibiotics were started, and she ultimately improved on a longer course of NSAIDs.

## Discussion

### *Background*

Chronic recurrent multifocal osteomyelitis (CRMO) is a relapsing autoinflammatory bone disorder that typically presents in childhood with low-grade fevers, bone pain, and localized swelling over affected bones. Radiographic imaging is suggestive of osteomyelitis. There have been approximately 400 pediatric cases reported in the literature [1], although the true prevalence is unknown and the disorder may be underdiagnosed. CRMO has also been referred to as chronic nonbacterial osteomyelitis or nonbacterial osteitis, but the term CRMO is more accurate and universally accepted in the literature [2]. The median age at diagnosis is typically 9–11 years of age, and females are more commonly affected [3–5]. Clinical course is significant for prolonged bone pain with remissions and relapses over several years with an approximate duration of active disease for 5–6 years [6]. CRMO is classified as an autoinflammatory process characterized by periods of systemic inflammation without evidence of autoantibodies, microorganisms, or antigen-specific T cells [7]. It has been associated with a multitude of inflammatory conditions including palmoplantar pustulosis, psoriasis, arthritis, sacroiliitis, inflammatory bowel disease, and Sweet syndrome [6, 8]. Another disorder characterized by chronic noninfectious osteomyelitis is synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) syndrome, which is more common in adults. At this time it is not clear if CRMO and SAPHO are separate clinical entities or reflective of varying spectrum of disease based on age [9].

## *Diagnosis*

The diagnosis of CRMO is relatively rare in published literature and may be misdiagnosed as bacterial osteomyelitis. Misdiagnosis may lead to unnecessary antibiotic therapy, imaging, and repeat bone biopsies prior to a proper diagnosis. Patients may experience a 15-month to 2-year delay in diagnosis [4, 10]. Pain is a consistent symptom and is often insidious [2, 5]. Laboratory evaluation may be normal or consistent with mild elevation of ESR, CRP, or complete blood count [4]. No definitive diagnostic criteria exist although proposed criteria from Manson et al. [11] in 1989 include (A) ≥ 2 radiographically confirmed bone lesions, (B) at least 6 months of remissions and exacerbations of signs and symptoms, (C) radiographic and bone scan evidence of osteomyelitis, (D) lack of response to antimicrobial therapy of at least 1-month duration, and (E) lack of an identifiable cause. To potentially avoid a long course of antibiotic therapy, Roderick et al. [4] in 2016 proposed the Bristol criteria which include the presence of typical clinical findings (bone pain ± localized swelling without significant local or systemic features of inflammation or infection) and the presence of typical radiological findings plus one of the following two criteria:

A. More than one bone (or clavicle alone) without significantly raised CRP (CRP < 30 g/L)
B. Unifocal disease (other than clavicle), or CRP > 30 g/L, with bone biopsy showing inflammatory changes with no bacterial growth while on antibiotic therapy

Radiographic imaging is suggestive of osteomyelitis, although lesions are typically multifocal and can occur in any bone. Commonly affected sites include metaphysis of the long bones, pelvis, spine, clavicle, and mandible [6]. Smaller bones of the hands and feet have been implicated, and clavicular involvement is considered a classic presentation and is suspicious for CRMO [2, 3]. Lesions may be lytic, sclerotic, or mixed and appear radiolucent with reactive and concurrent soft tissue swelling [5]. MRI may be useful to determine the

extent and evolution of disease [12]. Radionuclide bone scans have been used to identify asymptomatic lesions in other bones, although some experts suggest whole body (WB) MRI, especially in children, for diagnosis and detection of asymptomatic lesions [13]. WB MRI commonly reveals spinal involvement [2]. CRMO can mimic acute hematogenous osteomyelitis, such as staphylococcal osteomyelitis, as well as other childhood disorders with multifocal bony lesions, such as neuroblastoma, Langerhans histiocytosis, bone tumors, and leukemia. Ultimately, CRMO is a diagnosis of exclusion and commonly requires a bone biopsy to exclude other diseases.

## *Treatment*

An infectious etiology has not been established, and treatment with a wide range of antibiotics has been unsuccessful. There is broad agreement among orthopedic, infectious disease, and rheumatologic experts that antibiotics have no effect on the clinical course of CRMO. Anecdotal reports and case series advocate for treatment with NSAIDs or corticosteroids, with some studies preferring NSAIDs over corticosteroids [14]. Other therapies for cases of CRMO refractory to NSAIDs or corticosteroids include colchicine, bisphosphonates, interferon-gamma, interferon-alpha, and infliximab [15–17]. Literature on the use of bisphosphonates (mainly pamidronate) to reduce pain and improve function is growing [2]. Some experts recommend early use in children with spinal lesions as MR imaging after pamidronate therapy has shown improvement in vertebral modeling and height [17]. A majority of children diagnosed with CRMO have good clinical outcomes without significant sequelae although published studies of long-term follow-up are lacking. There is 1 long-term follow-up study of 23 patients, which found that 26% of patients had active disease at a median time of 13 years from diagnosis, while nearly half had bony deformities (leg length discrepancy

or bony overgrowth) 2 of which required surgery [6]. Another follow-up study of 17 patients found that patients in clinical remission may still have active lesions on WB-MRI [18]. Less favorable outcomes have been associated with multiple sites of involvement at onset and/or young age [19].

## *Back to Our Case*

In this patient's case, the multifocal pattern of bone lesions, sterile bone cultures, and relapsing symptoms are all consistent with CRMO. She responded well to NSAIDs without antibiotic therapy. She was suspected to have CRMO early in her clinical presentation, although she did undergo two bone biopsies to exclude other diagnoses. She was evaluated by orthopedic and pediatric infectious disease physicians, but her care was primarily managed by a pediatric rheumatologist.

**Clinical Pearls**

1. Chronic recurrent multifocal osteomyelitis (CRMO) is a culture-negative, relapsing multifocal osteomyelitis primarily affecting children and adolescents.
2. A multifocal pattern of bony lesions in the long bones, spine, or unusual sites such as the clavicle is suggestive of CRMO.
3. Bone biopsy may help further delineate the diagnosis and exclude other causes of multifocal bone disease in children, such as staphylococcal osteomyelitis or malignancy.
4. Treatment with antibiotics has no known effect on the clinical course or outcome.

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# Chapter 16
# Antimicrobial Dosing in the Elderly Population

**Montgomery W. Green and Michael E. Wright**

## Patient Case

An 80-year-old female is admitted to the hospital from a local nursing home with complaints of lower back pain. The patient has been experiencing localized lower back pain for the past 30 days per nursing home staff. She reports that the pain is often worse when she walks to the cafeteria for meals and is relieved with rest. The patient was treated with a 5-day course of trimethoprim-sulfamethoxazole for a presumed urinary tract infection. This course was completed 2 days ago. She reports no urinary symptoms but continued lower back pain.

**PMH** Bradycardia with pacemaker placement 90 days ago, osteoporosis, chronic kidney disease (baseline SCr 1.3 mg/dL), hypertension, COPD.

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J. Reznicek et al. (eds.), *Musculoskeletal Infections*,
https://doi.org/10.1007/978-3-030-41150-3_16

**Physical Exam** Temperature 37.5 °C; pulse 68; respirations 12; blood pressure 122/78; 81 kg; 65 inches.

Lower back tender to palpation. Deep tendon reflexes 4/4.

**Laboratory Findings** WBC 13,000 /μl, BUN 25 mg/dL, serum creatinine 1.6 mg/dL, potassium 5.2 mEq/L, lactic acid 1.8 mmol/L, ESR 88 mm/hour, CRP 13 mg/dL.

**CT of the Lower Spine** Bony destruction around endplates of L2 and 3. No abscess noted.

Patient is started on empiric therapy with vancomycin on day 1 of admission and peripheral blood cultures are obtained. On day 3, peripheral blood cultures return with *Staphylococcus aureus* sensitive to clindamycin, vancomycin, sulfamethoxazole/trimethoprim, and tetracycline and resistant to penicillin and oxacillin. The decision is made to discharge the patient on vancomycin for 6 weeks with follow-up. Of note, patient's serum creatinine on discharge returned to baseline of 1.3 mg/dL.

**Question** Has this patient experienced any antibiotic-related adverse effects? What needs to be considered when determining a dose of vancomycin for discharge? How and when should vancomycin be monitored?

## Variability in Age-Related Changes

There are changes in physiology that affect drug therapy as patients age; however, significant inter-individual variability is present in the elderly population [1]. Advancing age is not associated with consistent changes in the pharmacokinetic/pharmacodynamic parameters of medications as this wide variability exists. Frailty may be more pertinent to assess the changes that may occur with antimicrobials as opposed to age alone [1]. Frailty is difficult to define; however, it is associated with reduced lean body mass, muscle loss, malnourishment, reduced function, and reduced endurance [1]. Frailty associated with advanced age may be more apparent with func-

tional decline, weight loss, weakness, and fatigue [1]. Although the pharmacokinetic and pharmacodynamic principles discussed below are often related to advancing age, it is important to assess and treat patients individually and take into account the degree of frailty and its effect on medication therapy [1, 2].

## *Antimicrobial Pharmacokinetic Considerations in the Elderly*

Pharmacokinetic principles of antimicrobial administration include evaluation of the absorption, distribution, metabolism, and excretion of antimicrobials. Various changes in absorption occur as patients age including decreased bioavailability of medications absorbed by active transport and decreased first-pass metabolism; however, these changes in absorption are not associated with significant effect on oral absorption of antimicrobials based on evidence [1, 3]. Peak concentrations of orally administered medications may be blunted, but total absorption is comparable [4]. Thus administration of antimicrobials orally in the appropriate clinical scenario should be relatively unaffected and is encouraged in the elderly population.

Distribution of antimicrobials in elderly patients is affected by changes in lean body mass and total body fat [5]. Body fat may be increased by approximately 40% in elderly patients which is associated with a loss in lean body mass [5]. Due to this change in fat-to-muscle ratio, elderly patients may be at risk for higher tissue concentrations of highly lipid-soluble drugs (e.g., fluoroquinolones and macrolides) [2, 6]. In contrast, this increase in body fat is associated with decreased volume of distribution of water-soluble drugs (e.g., beta-lactams and aminoglycosides) resulting in higher serum concentrations with these antimicrobials [1, 5, 6].

The liver is largely responsible for the metabolism of medications [1]. Changes in hepatic function due to age are a significant source of variability in elderly patients' response

to medications [1]. Several commonly used antimicrobials are eliminated primarily by hepatic metabolism, and there is no straightforward estimation to determine adjustment of dosages based on declining hepatic function [5]. Patients with declining hepatic function may be more at risk for adverse effects associated with these antimicrobials (including nafcillin, oxacillin, ceftriaxone, fluoroquinolones especially moxifloxacin, doxycycline, minocycline, and macrolides) [5].

Many medications are excreted from the body via the kidneys, and the decline of renal function associated with age is well documented [1, 5]. This reduction in renal function is caused by reduced renal blood flow, parenchymal mass (10% per decade), and loss of functional glomeruli [5]. However, up to one-third of "normal" (non-frail) adults of advanced age have no reduction in measured creatinine clearance; thus, renal function varies with age but age alone is not predictive of impaired renal function [1, 2]. Calculation of creatinine clearance via the Cockcroft and Gault equation is the recommended method to assess for dosing adjustments of most antimicrobials, and individualized assessment of the patient and calculation of creatinine clearance is the best practice for selecting appropriate doses in elderly patients [1, 3].

Cockcroft and Gault equation:

$$\mathrm{CrCl} = \frac{(140 - \mathrm{age})(\mathrm{Ideal\ body\ weight}^{*})(\times 0.85\ \mathrm{CrCl\ if\ female})}{72 \times \mathrm{serum\ creatinine}}$$

∗Use actual body weight if patient weighs less than ideal body weight

Treatment of elderly patients with antimicrobials can be influenced by decreased renal function, alteration of distribution, and slow or decreased metabolism [2, 4, 7]. These factors are less likely to be associated with treatment failure but rather are concerning for an increased risk of adverse drug reactions in the elderly population [2, 7].

## *Antimicrobial Pharmacodynamic Considerations in the Elderly*

The pharmacodynamic properties of antimicrobials explain the relationship of the serum concentration and the extent that the medication is able to interact with the target as measured by the minimum inhibitory concentration (MIC) [3]. The changes in pharmacodynamic properties in elderly patients are complex and difficult to clearly define but may be associated with an altered drug response or increased sensitivity to medications [1]. Clinical success of antimicrobials is dependent upon whether the antimicrobial displays time- or concentration-dependent killing [2, 3]. The time over the MIC is the primary predictor of success for an antimicrobial displaying time-dependent pharmacokinetics [2]. If dose adjustments are necessary for these antimicrobials (e.g., beta-lactams), optimally dosing should be adjusted to allow for smaller doses administered more frequently [2]. In contrast, the primary predictor of success for concentration-dependent antimicrobials is the peak concentration achieved in the plasma [2]. Dose adjustments of these antimicrobials (e.g., aminoglycosides and fluoroquinolones) should involve higher doses administered less frequently [2].

## *Specific Antimicrobial Considerations*

### β-Lactam Antibiotics

As discussed previously, β-lactam antibiotics are time-dependent and dosing regimens should be designed to optimize this parameter [2]. As such, β-lactams are often administered multiple times per day, and certain β-lactams may be administered as a continuous infusion to ensure compliance and optimize this pharmacokinetic parameter [2]. Many of the antibiotics in this class are cleared renally; thus dose adjustments may be necessary, and if necessary, often a reduction of the dose while maintaining the frequency of administration is recommended [8].

There is some data supporting increased risk of seizures and rash in elderly patients on β-lactams [8]. Age-related reductions in serum albumin may increase the risk for toxicity of some β-lactam antibiotics that are highly protein bound [5]. Renal function should be monitored closely in elderly patients on cefepime and imipenem as these patients may be more predisposed to adverse effects. Cefepime is associated with a higher risk of encephalopathy in elderly patients with renal impairment [9]. Imipenem is associated with an increased risk of adverse reactions including a rare risk of seizures in patients who are predisposed [2]. Overall, β-lactam antibiotics have a favorable pharmacokinetic profile and are relatively safe in elderly patients [8].

## Vancomycin

Elderly adults have several altered physiological variables that affect vancomycin dosing and monitoring [10]. Renal impairment and increased incidence of obesity in the elderly make dosing vancomycin in the elderly somewhat nuanced. As a normal function of aging, the size and function of the kidney decreases substantially in some cases up to 25%. Vancomycin clearance is directly proportional renal function as 90% of vancomycin is excreted unchanged in the urine [10]. The average vancomycin half-life ($t_{1/2}$) in the elderly population is 17.8 hours. This is significantly longer than a middle-aged adult's average $t_{1/2}$ of 7.5 hours. The increase in $t_{1/2}$ is directly related to reduced clearance and increased volume of distribution (0.93 L/kg) in the elderly [10]. Estimating renal function in the elderly when dosing vancomycin is somewhat difficult as well due to the fact that the Cockcroft and Gault (CG) and Modification of Diet in Renal Disease (MDRD) formulas consistently over- or underestimate medication clearance, respectively [10]. A more accurate option (10% underestimation of renal function) has been described in the literature and is referred to as an optimized CG equation. The optimized CG equation uses the traditional CG equation with the lesser of actual body weight or ideal body

weight and caps the serum creatinine at a minimum of 0.68 mg/dL [10]. Target trough attainment is important in the elderly with trough concentrations of 15–20 mcg/mL being desirable for efficacious treatment of most MRSA infections. Troughs of greater than 25 mcg/mL have been correlated with toxicity. Vancomycin-associated nephrotoxicity is more common in patients 65 years of age and older with a cited incidence of 34% [11].

For severe MRSA infections, it is reasonable to use an initial vancomycin loading dose of 25–30 mg/kg based on actual body weight. However, it would be considered prudent to reduce empiric vancomycin maintenance doses. Consider rounding empiric maintenance doses down to the next available dose if your institution has a dose rounding policy or weight-based dosing at 10–15 mg/kg [12]. In patients with stable renal function, vancomycin serum trough concentrations should be collected before the fourth dose. After a therapeutic trough concentration is achieved, consider rechecking the trough once weekly in patients with stable renal function. In patients with rapidly changing renal function, consider collecting an initial vancomycin concentration sooner and monitoring continued therapy more frequently than weekly.

## Trimethoprim-Sulfamethoxazole

Trimethoprim-sulfamethoxazole (TMP-SMZ) is commonly cited as one of the most common antibiotics implicated in adverse drug reactions [5]. Concerns with TMP-SMZ not only include risk of rash and allergic reaction but also neutropenia, hyperkalemia, and renal dysfunction as well as several drug-drug interactions [4, 5, 13]. Elderly patients are more likely to experience neutropenia with TMP-SMZ [4]. Trimethoprim inhibits the secretion of potassium in the distal renal tubule which can result in hyperkalemia, and there is a concern for the concomitant use of TMP-SMZ with medications that can also increase potassium. A case-control study published by Antoniou and colleagues of patients

age 66 years and older prescribed TMP-SMZ while on concomitant spironolactone found a twofold increased risk of sudden death (adjusted OR 2.46, 95% confidence interval 1.55–3.90) within 14 days after exposure to TMP-SMZ [14]. TMP-SMZ is associated with nephrotoxicity, and the incidence of this has been reported as low in post-marketing studies [15]. One study performed by Varoquaux and colleagues compared the pharmacokinetics of TMP-SMZ in six young (29.3 ± 4.4 years) and six elderly (78.6 ± 6.6 years) patients [13]. Patients with a history of cardiac, renal hepatic, or gastrointestinal disease and those on major medical treatments were excluded. The authors found that renal clearance of TMP was significantly lower as well as higher serum concentrations of TMP in the elderly subjects despite normal baseline renal function. Fraser and colleagues evaluated the incidence of renal toxicity in middle-aged (average age of 65 years) veterans who received ≥6 days of TMP-SMZ [15]. Serum creatinine values obtained during therapy and within 3 days after completion of TMP-SMZ were evaluated. The authors found an 11.2% incidence of acute kidney injury (AKI) in the study, and 95% of the cases of AKI were deemed to be likely or possibly due to the use of TMP-SMZ. All but one of the cases of AKI resolved with discontinuation of TMP-SMZ and a multivariate analysis found that patients with hypertension and diabetes mellitus had an increased risk for experiencing AKI [15].

Drug interactions of concern with TMP-SMZ include warfarin, phenytoin, and sulfonylureas. TMP-SMZ inhibits the metabolism of warfarin and is well known to increase the international normalized ratio (INR) and risk for hemorrhage in a patient on warfarin [5]. There is an increased risk of phenytoin toxicity as TMP-SMZ inhibits the metabolism of this medication as well. Finally, the addition of TMP-SMZ to a patient's medication regimen with concomitant sulfonylureas (e.g., glipizide, glyburide, and glimepiride) may contribute to the increased risk for hypoglycemia in elderly patients [5].

## Aminoglycosides

Aminoglycosides utilization has waned over the last several years due to the development of less toxic antimicrobials with activity against highly resistant gram-negative organisms. Rates of nephrotoxicity have been reported as high as 24% in patients receiving aminoglycosides [16]. Standard consolidated (extended interval) dosing of aminoglycosides is recommended in the elderly, but only after careful evaluation of renal function. Reduced muscle mass in the elderly may result in overestimation of renal function when using CG formula. Consider the patients' weight and muscle mass individually when estimating renal function. Monitor renal function closely while in the inpatient setting by careful assessment of serum creatinine and urine output [3]. When possible discontinue nephrotoxic medications (i.e., angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, vancomycin, loop diuretics, and nonsteroidal anti-inflammatories) before initiating aminoglycoside therapy [17].

## Fluoroquinolones

Fluoroquinolones are commonly used in the elderly for a variety of indications ranging from pyelonephritis to gram-negative bacteremia. However, fluoroquinolones are associated with several adverse events that are more common in patients with impaired renal function including the elderly population. Some of the more serious adverse events associated with fluoroquinolones include but are not limited to agitation, prolonged Q-T interval, hypoglycemia, hepatitis, tendon rupture, and aortic aneurysm or dissection [18]. The majority of fluoroquinolones are excreted as unchanged molecules in the urine and undergo negligible hepatic metabolism [19]. Dose adjustments for all fluoroquinolones are recommended for patients with renal insufficiency with the exception of moxifloxacin. As mentioned previously, since

fluoroquinolones are concentration-dependent antibiotics, dose adjustments when necessary for patients with renal insufficiency should be made to maximize the peak concentration of the medication while decreasing the frequency. Consult the official prescribing information for the specific fluoroquinolone to ensure proper dosing for patients with renal insufficiency. Due to concerns with adverse effects in the elderly population, fluoroquinolones should be used with caution in this patient population.

**Clinical Pearls**

1. Significant inter-individual variability is found in the physiological changes that occur with advancing age. Patients should be assessed individually for dose adjustments and risk of adverse effects of antimicrobials.
2. Decreased renal function, altered distribution, and slow or decreased metabolism can affect antimicrobial therapy in elderly patients. These factors are more likely to affect the adverse effect profile of antimicrobials than treatment efficacy.
3. Renal function should be assessed with the calculation of creatinine clearance using the Cockcroft and Gault equation to determine appropriate dose adjustments for antimicrobials.
4. Trimethoprim-sulfamethoxazole, fluoroquinolones, and aminoglycosides should be used with caution in elderly patients, and patients should be closely monitored for adverse effects.
5. Vancomycin dosing should account for potential decreasing renal function with advanced age, and adjustments should be made based on measured trough concentrations.
6. Beta-lactam antibiotics have a favorable pharmacokinetic profile and are relatively safe in elderly patients.

## Patient Case Considerations

The patient presented in the case has likely experienced adverse reactions to the course of TMP-SMZ that she received for a possible urinary tract infection including increased serum creatinine and potassium. Vancomycin will be the most appropriate treatment option for this patient's bacteremia and vertebral osteomyelitis based on the culture data. To determine the appropriate vancomycin dose for discharge, the CG equation should be used to determine the patient's renal function. A trough should be obtained prior to the fourth dose of vancomycin and weekly thereafter (granted renal function remains stable). A trough goal of 15–20 is recommended for this patient's infection.

Calculated creatinine clearance for this patient using the CG equation is approximately 36 ml/minutes. Therefore, a dose of vancomycin of 1250 mg Q24H would be appropriate based on an estimated dose of 15 mg/kg and frequency dependent upon her creatinine clearance.

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# Chapter 17
# Necrotizing Fasciitis

**Paul W. Perdue, Jr.**

## Case

A 62-year-old homeless male with a past medical history of poorly controlled diabetes mellitus (hemoglobin A1C of 9%), hypertension, peripheral vascular disease and intravenous drug use presented to the emergency room after 4 days of worsening right leg pain with associated redness and swelling. He also endorsed subjective fevers and chills. The patient reported a minor trauma to the leg after striking it on a table approximately 1 week prior to presentation. His last visit to a primary care physician was approximately 2 years ago.

On physical examination the patient's vital signs were: temperature 102.1 °F, blood pressure 95/60, heart rate 125 beats/minute and oxygen saturation of 96% on 2L nasal cannula. He appeared to be in significant discomfort with slightly labored breathing. He was also disoriented to place and time. Further focused evaluation of the right lower extremity demonstrated significant swelling and discoloration of the proximal aspect of the leg below the knee. There was further redness, erythema and associated warmth extend-

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J. Reznicek et al. (eds.), *Musculoskeletal Infections*,
https://doi.org/10.1007/978-3-030-41150-3_17

ing proximally and distally. There were visible bullae with palpable crepitus about the discolored region and significant tenderness to palpation along the entire leg. A clinical photograph of the right lower extremity is shown in Fig. 17.1.

Pertinent laboratory values:

- Sodium: 128 mmol/L
- Glucose: 405 mg/dL
- Creatinine: 2.3 mg/dL
- Lactate: 4.5 mmol/L
- C-reactive protein (CRP): >31 mg/dL
- White blood cell (WBC) count: 29.1 ($\times 10^9$/L)
- Hemoglobin: 10.7 g/dL
- Platelets: 249 ($\times 10^9$/L)
- Erythrocyte sedimentation rate: 113 mm in 1 hour
- INR: 1.2

Radiographs as well as computed tomography (CT) of the right leg were obtained and shown in Figs. 17.2, 17.3, and 17.4. Both the plain radiographs and CT scan demonstrated gas throughout the soft tissues of the lower leg.

Given the patient's clinical history, physical examination, laboratory results and imaging findings, he was diagnosed with necrotizing fasciitis of the right lower extremity. He was started on broad-spectrum intravenous (IV) antibiotics and taken emergently to the operating room for an extensive debridement of the extremity. Intraoperative findings consisted of avascular skin and subcutaneous tissue with the presence of foul-smelling "dishwater" fluid at the level of the deep fascia. The patient was managed in the intensive care unit postoperatively with further tailoring of IV antibiotics. The intraoperative cultures were positive for group A beta-hemolytic streptococci. Due to the extensive nature of the infection and after multiple further debridements, the patient subsequently underwent an above-the-knee amputation with eventual discharge to a skilled nursing facility on hospital day 27.

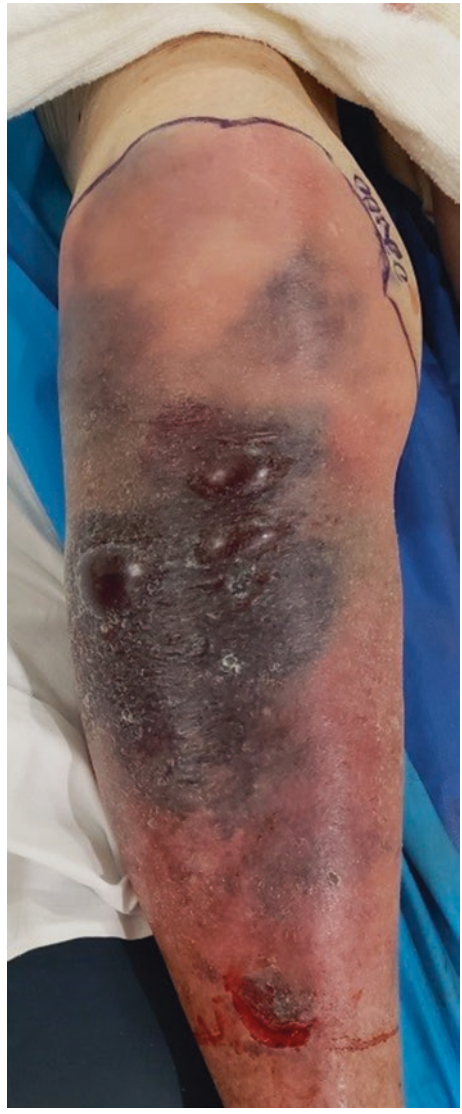

FIGURE 17.1
Clinical photograph of the right leg. Note the significant swelling and edema extending proximally and distally. Also note the blisters/bullae

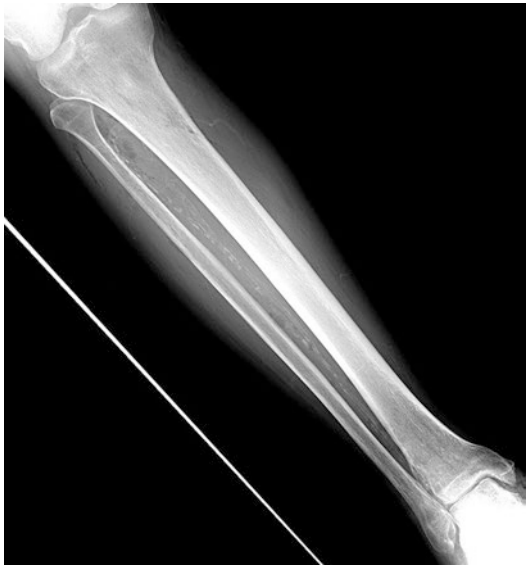

Figure 17.2 Anteroposterior radiograph of the affected extremity. Note the extensive air within the tissues. Also note the calcified arteries indicative of peripheral vascular disease

## Discussion

### *Background*

Necrotizing fasciitis (NF) is a bacterial infection that spreads along the fascial planes of involved tissue leading to progressive necrosis of the fascia and overlying subcutaneous tissue. It was described by Hippocrates in the fifth century BC and first reported in the United States in 1871 by Confederate Army surgeon Joseph Jones who referred to it as "hospital gangrene" [1]. Anatomic involvement is typically separated into two distinct areas, the trunk/perineal region and extremities, with the latter being most common [2]. It typically follows an injury to the involved site which can be as simple as

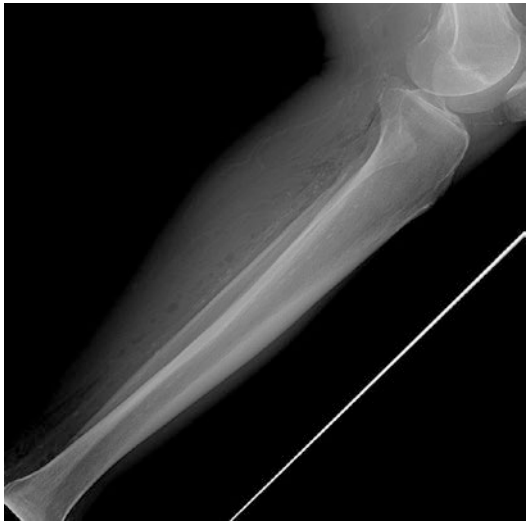

FIGURE 17.3 Lateral radiograph of the affected extremity. Again note the extensive air within the tissues posterior to the tibia

a "minor" contusion. Necrotizing fasciitis has also been associated with trauma, insect bites, surgical incisions, abrasions, ulcers, burns, penetrating injuries and muscle strains [3–5].

Necrotizing fasciitis is rare with an incidence of about 0.4 cases per 100,000 people in the United States [6]. Although conditions that lead to an immunocompromised state are risk factors for developing necrotizing fasciitis, about half of all cases occur in previously healthy individuals with no identifiable risk factors [4]. Diabetes mellitus is the most common comorbidity and associated with 18–60% of cases, while other comorbidities include obesity, peripheral vascular disease, intravenous drug use, alcohol abuse, smoking, malnutrition, chronic cardiac disease, chronic corticosteroid therapy and chronic immune suppression [3]. Early diagnosis is missed in up to 85–100% of cases and mortality rates still range from 6% to 76% [3, 6].

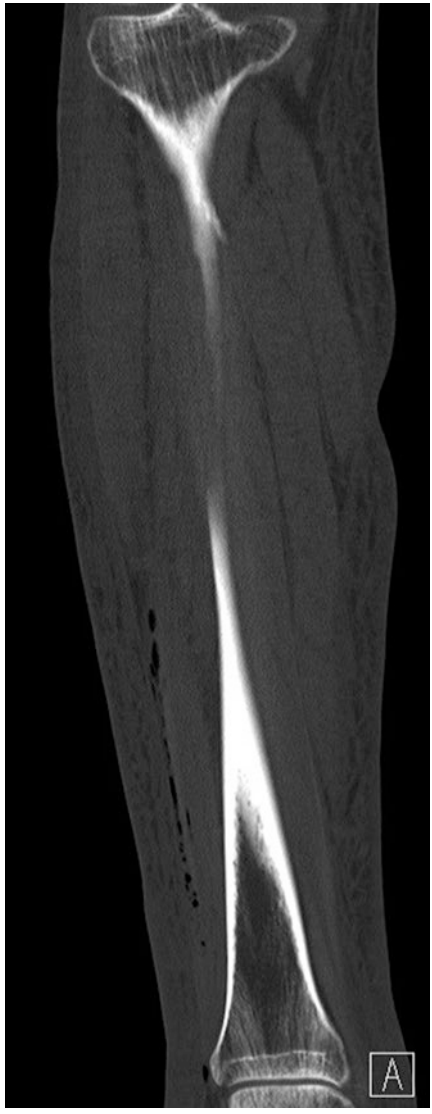


Figure 17.4 Coronal CT scan of the affected extremity. Note the air and subcutaneous tissue stranding/edema

## *Pathophysiology*

Entrance of bacteria into the subcutaneous tissue frequently occurs via external trauma (i.e., laceration, abrasion or burn) or from bowel perforation or perineal origin. The bacteria then proliferate and release various toxins and enzymes which allows further extension of the infection along fascial planes. Progression of the infection leads to venous and arterial occlusion, resulting in subcutaneous tissue and skin ischemia. At this point bullae may form with eventual ulceration and necrosis of the skin. The development of ischemia and necrosis activates a massive inflammatory response which can then lead to multi-organ failure and death.

## *Clinical Presentation*

Necrotizing fasciitis typically begins as an area of localized inflammation or erythema which may or may not involve prior contusion or trauma. At this point in the disease progression it may be incorrectly diagnosed as cellulitis. A "triad of swelling, erythema and inordinate pain" should raise suspicion for a diagnosis of NF [3]. Subsequent rapid progression of the erythematous margins is characteristic of the early stage of the disease process [7].

As NF progresses, the traditional or classic signs may begin to develop. These include blisters or bullae formation as well as skin discoloration. Although commonly associated with NF, one series demonstrated that the classical bullae and necrosis only occurred in 47% of patients and only 51% were febrile [8]. Crepitus may also be present due to gas development within the soft tissues. Soft tissue edema and pain continue to worsen. Disproportionate pain is considered the most sensitive symptom being noted in almost 100% of patients with NF [9]. The characteristic foul-smelling "dishwater fluid" develops secondary to necrosis of the superficial fat. Fever, chills, hypotension and altered level of consciousness/mental status may also develop.

## *Diagnosis*

Diagnosis of NF is mostly clinical, but laboratory tests and imaging can assist with confirmation of the diagnosis. Most importantly, obtaining these studies should not delay emergent surgical intervention. Initial laboratory evaluation should include a complete blood count, comprehensive metabolic panel, C-reactive protein, and coagulation studies. Blood cultures can also be obtained in order to direct antibiotic therapy. Metabolic abnormalities may be minimal early in the disease process but can quickly manifest as the disease progresses to sepsis and multi-organ failure. Common abnormalities include azotemia, hyponatremia, hypoproteinemia, thrombocytopenia, hematuria, elevated C-reactive protein and erythrocyte sedimentation rate, anemia, hypoalbuminemia and metabolic acidosis [3]. Wong et al. developed the LRINEC (Laboratory Risk Indicator for Necrotizing Fasciitis) score which helps to differentiate NF from other soft tissue infections using specific laboratory parameters [10]. These parameters include CRP, WBC, hemoglobin, serum sodium, creatinine and glucose levels (Table 17.1). The combined LRINEC score assists in predicting the probability of NF with a score ≥8 having a 75% probability of being NF.

Imaging is also a useful adjunct in confirming the diagnosis of necrotizing fasciitis. Plain radiographs are simple, quick and easy to obtain. They may demonstrate the presence of gas in the soft tissues but may also be negative in the early stages of the infection. Computed tomography is also a useful study as it can demonstrate changes within the soft tissues and fascia, such as thickening or edema, as well as the presence of gas. Similar to plain radiographs, CT findings can be negative early in the infectious process and have been negative even in the presence of confirmed NF [9]. Magnetic resonance imaging (MRI) has also been shown to have a high sensitivity of 93–100% in the diagnosis of NF and demonstrates characteristic signs secondary to the liquefactive necrosis and inflam-

Table 17.1 Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC score)

| | | |
|---|---|---|
| CRP (mg/dL) | <15 | 0 |
| | >15 | 4 |
| WBC (per $mm^3$) | <15 | 0 |
| | 15–25 | 1 |
| | >25 | 2 |
| Hemoglobin (g/dL) | >13.5 | 0 |
| | 11–13.5 | 1 |
| | <11 | 2 |
| Sodium (mEq/L) | ≥135 | 0 |
| | <135 | 2 |
| Creatinine (mg/dL) | ≤1.6 | 0 |
| | >1.6 | 2 |
| Glucose (mg/dL) | ≤180 | 0 |
| | >180 | 1 |
| Total score | <6 | Low risk |
| | 6–7 | Intermediate risk |
| | ≥8 | High risk |

matory edema that creates fascial fluid [9]. Although MRI can be a useful tool in identifying the extent and borders of the infection, surgical intervention should not be delayed solely to obtain the MRI.

Biopsy is also a possible bedside tool that can be utilized to diagnose NF. The "finger test" can be performed at the bedside and involves local anesthesia with a small incision. A gloved finger is then inserted to the deep fascia, and the presence of "dishwater fluid," lack of bleeding, and lack of tissue resistance define a positive test [3]. Frozen-section biopsy can also be obtained and allows for quick diagnosis but requires an experienced pathologist to be available [11]. Similar to obtaining advanced imaging, obtaining a biopsy should not delay surgical debridement when the diagnosis of NF is suspected.

## *Classification*

Necrotizing fasciitis infections can be classified according to the gram stain and culture results. Type 1 is the most common, 55–90% of cases, and involves a polymicrobial infection [12]. They are typically postoperative trunk or perineal infections (Fournier gangrene). Multiple bacterial species are cultured from the wound including non-group A *Streptococcus*, anaerobes and *Enterobacteriaceae*. Virulence is thought to be due to synergy between the bacterial species [3].

Type 2 NF is monomicrobial and associated with the presence of group A beta-hemolytic streptococci as the sole species, although other organisms, such as *Staphylococcus aureus*, may be present [13]. These infections usually involve the extremity and can occur in previously healthy individuals. Group A *Streptococcus* is naturally present on the skin and mucosal surfaces. It has a tremendous ability to diversify and acquire prophages which then confers virulence through phage-associated factors and increases bacterial survival against the host [14]. Patients with Type 2 NF can experience rapid progression of the infection with development of septic shock and multi-organ failure [15].

Type 3 NF is secondary to marine exposures, such as contaminated wounds or seafood ingestion, with *Vibrio vulnificus* or *Aeromonas hydrophila* being the most common isolated pathogens [13]. Type 4 NF is more common in immunocompromised patients, specifically those with extensive burns, and is secondary to fungal pathogens, such as *Candida* species or *Zygomycetes*.

## *Treatment*

Initial treatment of NF relies on early identification and diagnosis. The diagnosis can be made based on history, clinical examination and laboratory findings. Imaging is a useful adjunct that can help to confirm a diagnosis but can be negative in the early stages of the infection. Early diagnosis allows

for early surgical debridement which is the basis of management of NF. Early debridement is the best way to reduce and eradicate the bacteria and stop the necrotic process that eventually leads to a systemic inflammatory response, sepsis and death. The goal of the first debridement is to remove all necrotic tissue which has been shown to be the only intervention that increases survival rates [2, 4]. Skin, subcutaneous tissue, muscle and fascia are debrided of all necrotic tissue until healthy bleeding tissue is identified. In select cases of aggressive infection, immediate amputation is necessary as a lifesaving procedure, although some studies have shown that amputation does not improve mortality [16]. Daily evaluations of the wound are necessary and repeat debridements are common. Once the infection has been eradicated, wound coverage can be addressed, many times with involvement of the plastic surgery team.

Antibiotic therapy is an important facet in the treatment of NF. The fascia is poorly vascularized, therefore combined surgical and antibiotic therapy is necessary to treat the infection. Antibiotics help to reduce bacterial load, terminate toxin production and prevent organ failure [3]. Initial treatment should involve broad-spectrum antibiotics with activity against gram-positive, gram-negative and anaerobic organisms. Intraoperative cultures of purulent material and/or deep tissue allow for adjustment in antibiotic therapy based on speciation. Early administration of clindamycin is advocated when there is suspicion of group A streptococcal or *Staphylococcus aureus* infection due to its ability to inhibit ribosome function which then inhibits M protein and exotoxin production. Synthesis of tumor necrosis factor is suppressed which decreases the exaggerated immune response [3, 5]. Utilizing clindamycin in the treatment of necrotizing fasciitis has been shown to reduce hospital mortality by 89% [17]. Table 17.2 describes antibiotic management based on culture results.

Patients with NF also require aggressive fluid resuscitation and blood pressure support, typically in an intensive

Table 17.2 Antibiotic therapy for necrotizing fasciitis

| Antibiotic treatment for necrotizing fasciitis | | | |
|---|---|---|---|
| **Empiric therapy** | **Group A streptococci** | ***Staphylococcus aureus*** | ***Clostridium* species** |
| Vancomycin and clindamycin, plus one of the following:<br>Imipenem<br>Meropenem<br>Piperacillin/tazobactam<br>Cefepime + metronidazole | Penicillin + clindamycin | Nafcillin, cefazolin, or vancomycin (for resistant strains) + clindamycin | Penicillin + clindamycin |

care setting. Similar to burn victims, the large wounds from the debridements require specialized nutritional support and repletion. Although further study is still needed to prove efficacy, other adjunctive therapies that have been described include intravenous immunoglobulin G (IVIG), hyperbaric oxygen (HBO), and human-activated protein C [18–20].

## Gas Gangrene

Although sometimes the terms "gas gangrene" and "necrotizing fasciitis" are used interchangeably, they are two different types of infections that have different etiologies and characteristics. In spite of the differences, the definitive treatment for both consists of prompt surgical debridement and antibiotic therapy. Also known as clostridial myonecrosis, gas gangrene develops in devitalized tissue that has been crushed or sustained significant trauma. The traumatized tissue provides a medium for the infection to flourish and spread. It can be categorized as either being caused by *Clostridium* species or non-clostridial. Non-clostridial bacteria that can cause gas gangrene include *Escherichia coli*, *Pseudomonas* species, *Proteus* species and *Klebsiella pneumoniae* and tend to occur primarily in patients with diabetes [21]. Clinical examination

reveals similar findings to those found in necrotizing fasciitis including rapidly progressive and expanding erythema/edema, skin discoloration, severe pain and blister/bullae formation. Whereas "dishwater fluid" is characteristic to necrotizing fasciitis, true foul-smelling purulence is found in gas gangrene [21]. Imaging may reveal gas within the soft tissues and patients can rapidly develop renal failure due to muscle necrosis. Standard treatment relies upon extensive debridement with excision of all necrotic and infected tissue as well as antibiotics tailored to intraoperative culture speciation. Hyperbaric oxygen therapy is also another adjunctive treatment modality [22].

**Clinical Pearls**

1. Necrotizing fasciitis is a severe life-threatening infection that necessitates prompt diagnosis in order to initiate appropriate treatment.
2. Classical signs, such as blistering, bullae and fever, may or may not be present on physical examination.
3. Imaging modalities, such as plain radiographs and computed tomography, may help to confirm a diagnosis but could be negative in the early stages of the infectious process.
4. Diagnosis of necrotizing fasciitis is mainly clinical and advanced imaging and/or biopsies should not delay prompt surgical debridement.
5. The LRINEC score is a useful tool that utilizes specific laboratory values to predict the probability of necrotizing fasciitis.
6. Extensive surgical debridement in combination with antibiotic therapy is the mainstay of treatment for necrotizing fasciitis.
7. Gas gangrene, or clostridial myonecrosis, is a separate infection from necrotizing fasciitis.
8. Treatment of gas gangrene is similar to necrotizing fasciitis and includes prompt surgical debridement and antibiotic therapy.

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# Chapter 18
# Iliopsoas Abscess

**Jamie L. Engel and Jibanananda Satpathy**

## Case Report

A 61-year-old female with no significant medical history presented with acute onset of low back pain for 1 week. She worked for a newspaper. She noticed acute low back pain when trying to pick up something from the floor. She also noticed intermittent chills as well as bilateral lower extremity swelling. She had progressive difficulty in her daily activities and endorsed she had not eaten well for a week with significant weight loss. She presented to an outside hospital where a CT chest and abdomen as well as an ultrasound of her legs revealed bilateral lower extremity deep vein thrombosis associated with bilateral pulmonary embolism and bilateral large psoas abscesses with L4–L5 diskitis. She was transferred to our facility for further management.

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J. Reznicek et al. (eds.), *Musculoskeletal Infections*,
https://doi.org/10.1007/978-3-030-41150-3_18

On physical exam she looked cachectic with a BMI just over 15. She had fullness in bilateral flanks, associated with significant tenderness. Hip range of motion was painful, and she kept both legs flexed; extension produced significant pain. Her labs showed leukocytosis with a white blood cell count of 16.2, erythrocyte sedimentation rate of 112, and C-reactive protein of 17.7 (0.5 being normal high). She was found to be significantly malnourished with transferrin of 104 and absolute lymphocyte count of 1000.

Due to the nature of her symptoms and her history, both an MRI of her lumbar spine and a CT with contrast of his pelvis were performed. The MRI revealed L5-S1 diskitis with paravertebral abscess. The CT with contrast demonstrated massive bilateral psoas abscess (Figs. 18.1 and 18.2).

The abscess was surgically drained through bilateral iliofemoral approaches as the abscess extended into the thigh.

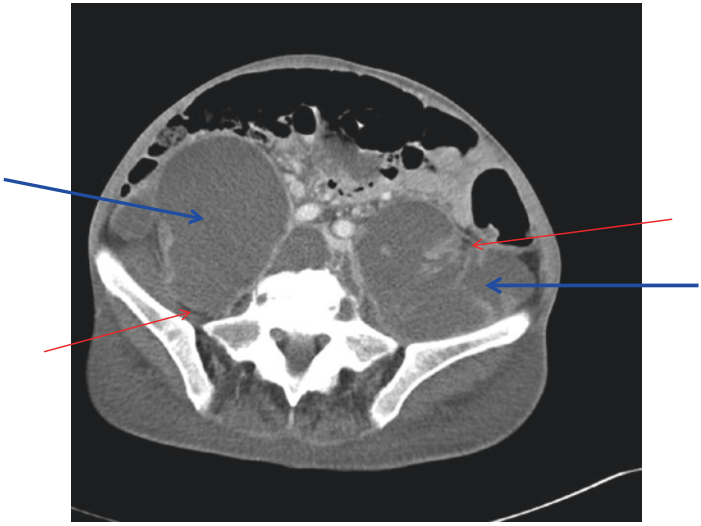

Figure 18.1 Axial CT cut showing bilateral massive psoas abscesses (blue arrows). These are seen as hypodense, ring-enhancing lesions. This CT cut also demonstrates air within the abscesses (red arrows), a common finding in iliopsoas abscesses

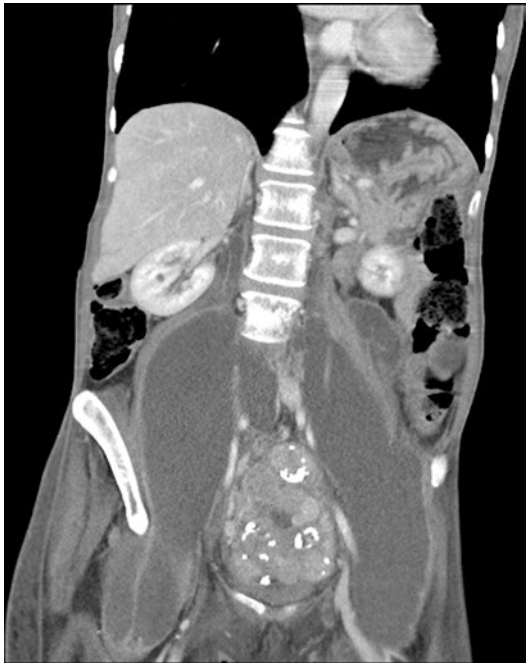

Figure 18.2 A coronal CT cut demonstrating bilateral, massive iliopsoas abscesses. Here the hypodense, ring-enhancing mass can be seen clearly following the anatomy of the iliopsoas musculature

Large amounts of purulent fluid were drained from the bilateral psoas abscesses. An indwelling suction drain was placed at the time of surgery. Neurosurgery performed a laminectomy and extensive debridement of L5-S1 area. The patient also was found to have an infected tooth that was subsequently extracted.

Her cultures grew *Streptococcus anginosus*. She was treated with 6 weeks of IV ceftriaxone. Also, metronidazole was added since *Strep. Anginosus* is typically involved with polymicrobial infection, especially anaerobes. The patient remains in a long-term care facility due to homelessness and overall poor mobility.

## Discussion

Psoas abscesses are classified by the source of the infection with primary infections being the result of hematogenous spread from a distant, often occult, source in the body. These are most commonly seen in patients with immunocompromise such as HIV or uncontrolled diabetes. The patient described here did not have any known comorbidity. Secondary infections include those that occur by direct spread of inflammation or infection from structures adjacent to the iliopsoas such as in the case of Crohn's disease, ulcerative colitis, diverticulitis, colorectal carcinoma, lumbar vertebral body osteomyelitis, mycotic aortic aneurysms, and complicated urinary tract infections and pyelonephritis [1, 2]. In the presented case, the likely source was an infected tooth with subsequent hematogenous spread to the spine and iliopsoas muscle.

Signs and symptoms of psoas abscesses are varied and inconsistent from patient to patient. The most commonly reported symptom is flank or back pain, which is seen in 50–90% of patients and was present in the patient here. The second most common presenting symptom is a fever, which is seen in 40–60% of patients and was also present in the reported patient [3–6]. A clinical triad of back/flank pain, fever, and limp was described, but this has subsequently been found to be present in only about 10% of patients with psoas abscesses [4, 5]. Other commonly reported symptoms include malaise, abdominal pain, limp, groin mass, weight loss, and loss of hip range of motion. Patients with a psoas abscess will typically hold their hip in flexion to take tension off the psoas muscle and have increased pain with passive extension of the hip. Patients with intraarticular hip pathology, such as a septic hip, will have the same response to position of the hip, and, thus, it is not a reliable diagnostic sign [1, 3, 5]. The patient here had the classic signs as described above.

Laboratory testing often reveals anemia and leukocytosis. Patients with psoas abscesses nearly universally have elevated inflammatory markers including C-reactive protein and

erythrocyte sedimentation rate [1]. Blood cultures should always be taken as abscess fluid only has growth in culture medium in about 75% of patients [2–5]. In these cases, positive blood cultures can be used to direct antibiotics. In this patient, abscess fluid cultured grew *Strep. anginosus*, which is a mouth bacterium. Subsequent exam of her tooth confirmed an infected tooth requiring extraction.

CT with contrast is the imaging modality of choice in these patients. MRI may also be used, especially to assess the spine. Also, CT-guided percutaneous drainage is a reasonable treatment choice for many of these abscesses, making a CT the preferred imaging modality. One issue to consider is that when CT or MRI are performed within 5 days of onset of symptoms, their sensitivities decrease to 50%; after 6 days of symptoms, the sensitivities of both modalities approach 100%. Plain radiographs may give some clues to the presence of a psoas abscess, such as gas shadows in the retroperitoneum or asymmetry of the psoas musculature, but they are not diagnostic (Fig. 18.3). Ultrasound is user dependent and can be obscured by bowel gas or body habitus [7].

Findings indicative of psoas abscess on CT include hypodense mass, gas or air fluid levels, rim enhancement of the abscess wall, and infiltration of surrounding fat. Cases of false-negative CTs are typically abscesses that do not attenuate or produce air. The case presented here demonstrated a hypodense mass infiltrated with air in and adjacent to the psoas musculature [7].

The first-line treatment for all psoas abscesses is broad-spectrum antibiotics. Until cultures and sensitivities are obtained, antibiotics should cover gram-positive and gram-negative organisms as well as gastrointestinal and genitourinary flora, unless the source of the abscess is known. Clindamycin, antistaphylococcal penicillin, metronidazole, and aminoglycosides should all be considered. If high suspicion for tuberculosis infection is present, antituberculous medications should be considered as well. These can be exchanged for pathogen-directed antibiotics as soon as cul-

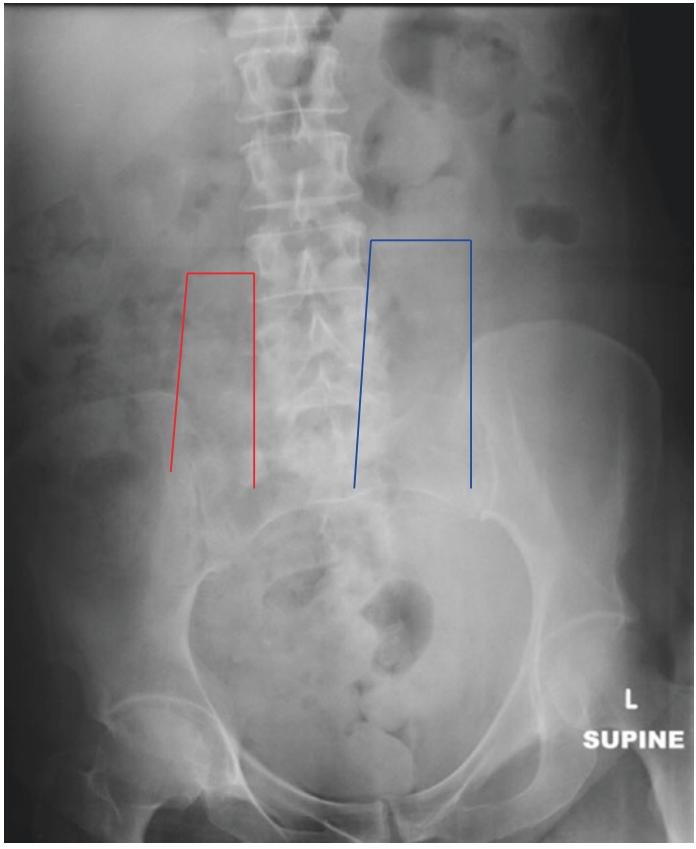


Figure 18.3 Abdominal x-ray demonstrating subtle radiographic findings of a psoas abscess. Here the psoas shadow is thicker on the left (blue outline) than the right (red outline). This finding is not sensitive or specific for a psoas abscess, but is an indication that advanced imaging is needed

tures and sensitivities are resulted. There is no consensus regarding length of antibiotic treatment, and reported durations vary from 2 weeks to 6 months. In the case of psoas abscess secondary to tuberculosis, antituberculous medications should be continued for 9 months to a year [3, 6].

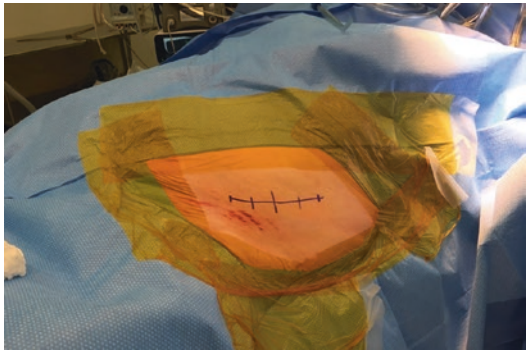

Figure 18.4 Incision for an anterior approach to the iliopsoas via the lateral window of an ilioinguinal approach to the pelvis. In this depiction, the patient is supine with the legs to the left and the head to the right. This is one of many surgical approaches that may be used for open drainage of an abscess

In addition to antibiotics, drainage of the abscess is needed. This can be done either in an open, surgical fashion (Fig. 18.4) or percutaneously with CT or ultrasound guidance. For small abscesses, antibiotics alone may be sufficient, but for large abscesses (greater than 3 cm), mortality may be as high as 100% without abscess drainage [8]. In the case of a secondary abscess, the source of the abscess should be addressed at the same time as the drainage of the psoas abscess to decrease the risk of recurrence. If a bowel resection and anastomosis is required to treat the primary source, a diversion should be performed first, followed by anastomosis at a later date, once infection has resolved [6].

The historical mortality rate of psoas abscesses has been high, with rates up to 44%, but this has fallen dramatically since the increase in widespread use of CT scans resulting in earlier diagnosis of abscesses. The mortality rate for primary abscess is now as low as 2.5%, while the rate for secondary abscesses remains relatively high at 19% [4, 9]. Mortality is typically related to delayed or inadequate treatment, and the most frequent cause of death is sepsis. Other complications

include recurrent abscess, septic hip, septic emboli, venous thromboembolic disease, and multidrug-resistant infections, among others [3].

**Clinical Pearls**

1. Psoas abscesses have inconsistent clinical signs and symptoms and should be considered in the differential diagnosis for patients with back or flank pain, especially if inflammatory markers are elevated.
2. Contrast-enhanced CT scan is the gold standard for diagnosis of psoas abscesses.
3. When imaging is obtained within 5 days of the onset of symptoms, the sensitivity of all modalities drops dramatically. If suspicion for an abscess remains high with negative imaging, it should be repeated.
4. The most effective treatment of these infections is a combination of antibiotics and drainage.
5. Drainage may be surgical or CT guided, but in the case of secondary abscess, it is important to address the source of the infection, which may require surgical intervention.
6. While mortality rates for psoas abscess are dropping, they are still high, especially in the case of secondary abscesses. The rate is decreased by early diagnosis and aggressive debridement.

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# Chapter 19
# *Staphylococcus aureus* Skin Infections

**Jonathan K. Pan and Julie Reznicek**

## Case

A 46-year-old African-American male is brought to the emergency department from his prison facility due to several days of an enlarging, painful nodule on his left anterior thigh with surrounding erythema. The patient tells the emergency room physician that he has had these "bumps" before and he was told they were "spider bites." His medical comorbidities include hypertension and tobacco dependence. He denies any systemic symptoms such as fever or rigors. On exam, there is a fluctuant 3 cm nodule on his left anterior thigh with a 2 cm area of surrounding erythema. The patient is diagnosed with an abscess and it is incised and drained at bedside. The purulent material is sent for bacterial cultures. Preliminary gram stain is shown below (Fig. 19.1). The incision is packed and he is given a 10-day course of doxycycline.

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J. Reznicek et al. (eds.), *Musculoskeletal Infections*,
https://doi.org/10.1007/978-3-030-41150-3_19

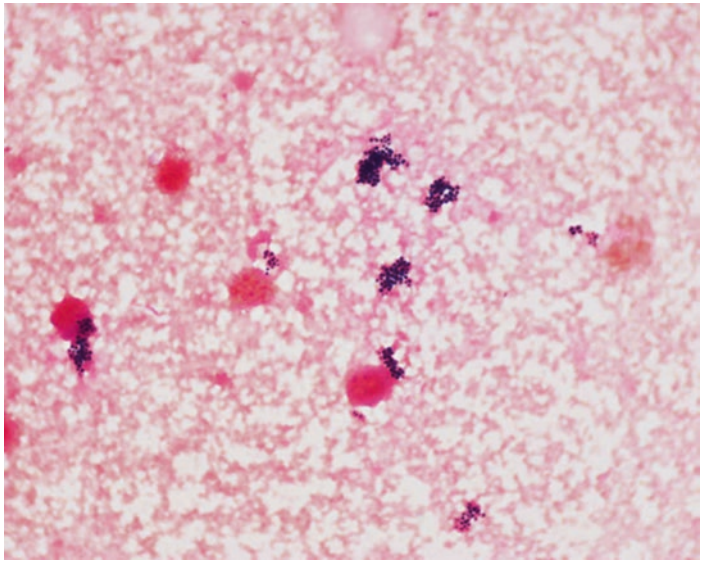

Figure 19.1 Gram stain at 1000× magnification. (Photo courtesy of Alexandra Bryson, Ph.D., D (ABMM))

## Introduction

Skin and soft tissue infections (SSTIs), including impetigo, cellulitis, and cutaneous abscesses, comprise up to 3% of all emergency department encounters in the USA. Identification of a causative pathogen may be difficult, especially in the case of cellulitis, but when an appropriate microbiological sample can be obtained, *Staphylococcus aureus (S. aureus)* is the most prevalent pathogen identified [1–3].

*Staphylococcus aureus* was first isolated in a surgical site infection in the late 1800s. The name "aureus," meaning "golden" in Latin, was assigned to this organism because of the color of the beta-hemolytic colonies seen on a blood agar culture plate. Initial suspicion of *S. aureus* often arises after routine crystal violet staining reveals distinctive gram-positive

(purple) cocci in "grapelike" clusters. *S. aureus*, which is both aerobic and facultatively anaerobic, also demonstrates a positive catalase test. Biochemical testing can further distinguish *S. aureus* from other *Staphylococcus* species, with a positive coagulase test in *S. aureus* and negative in other staphylococcal species [4].

Since its discovery as a nosocomial pathogen in the 1960s, methicillin-resistant *Staphylococcus aureus* (MRSA) has played an increasing role in both hospital- and community-acquired skin and soft tissue infections [5]. Studies have demonstrated that nearly 50% of all SSTIs, including abscesses, involve MRSA [1, 6–8].

## The Backbone of Resistance in MRSA Strains

MRSA owes its resilience to the production of an altered penicillin-binding protein, PBP2A, an essential enzyme that catalyzes the production of peptidoglycan in the bacterial cell wall. PBP2A has a lower affinity to bind to beta-lactams (and other penicillin-derived antibiotics) when compared to other PBPs [9, 10]. This alteration allows MRSA to survive when exposed to many of the beta-lactam antibiotics, including methicillin, nafcillin, oxacillin, and most cephalosporins [5, 9–11]. PBP2A is encoded by the *mecA* gene, which can be found on a mobile genetic element called the staphylococcal cassette chromosome *mec* (SCC*mec*). This SCCmec is inserted and integrated into the bacterial chromosome. There are currently 13 types of SCCmec elements classified based on the gene complexes they carry.

Studies have observed that hospital-acquired MRSA (HA-MRSA) isolates more commonly carry the larger SCCmec types I, II, and III, while community-acquired MRSA (CA-MRSA) isolates often carry the smaller SCCmec types IV and V [12–14].

## *Epidemiology of CA-MRSA SSTIs*

Though initially isolated in critically ill hospitalized patients, MRSA soon emerged as a significant pathogen in the community, infecting younger and typically healthier hosts, with no prior exposure to a healthcare environment [5, 14, 15]. This new strain of MRSA, deemed community-associated MRSA (CA-MRSA), was also unique in its increased susceptibility to non-beta-lactam antibiotics compared to its healthcare-associated MRSA (HA-MRSA) counterpart [5]. The distinction of CA-MRSA was initially defined by the CDC based on epidemiologic factors: a MRSA infection within 48 hours of admission in a person without exposure to healthcare facilities in the past year and without indwelling lines. Molecular techniques have now identified genotypic differences between CA-MRSA and HA-MRSA strains. Such advances led to the detection of one particular strain of MRSA that became the predominant pathogen among CA-MRSA infections in the USA. This strain, named USA-300, continues to account for the majority of community-associated MRSA spontaneous skin and soft tissue infections in this country [16, 17]. Outbreaks, both nationally and internationally, have also been attributed to this particular MRSA stain [18, 19]. Although unique genetic elements have been linked to the USA-300 stain, specifically a smaller SCCmec IV element and the gene for production of cytoxin Panton-Valentine leukocidin (PVL), the exact role that these play in the global emergence of this strain remains controversial [14].

Besides epidemiologic and genotypic distinctions between HA and CA strains of MRSA, there are also distinguishing clinical characteristics. CA-MRSA is predominantly associated with SSTIs, while HA-MRSA has a propensity for more invasive syndromes including pneumonia and bacteremia. Not surprisingly, the distinction between CA- and HA-MRSA infection is becoming increasingly blurred. Not only do HA-MRSA strains circulate among the community, but CA-MRSA has been increasingly isolated in invasive nosocomial infections [14]. Molecular techniques may also be of

decreasing value in this regard as well, as emerging evidence demonstrates that MRSA may accumulate multiple SCCmec elements [12].

## *Treatment*

The 2011 Clinical Practice Guidelines by the Infectious Diseases Society of America (IDSA) for the Treatment of Methicillin-Resistant *Staphylococcus aureus* Infections in Adults and Children state that incision and drainage (I&D) alone for simple abscesses is likely adequate, citing several small studies demonstrating no improvement in cure rates with the addition of systemic antibiotics [20]. Larger studies have since been published demonstrating improved cure rates and decreased recurrence when oral antibiotics are given alongside I&D, even in the setting of small, uncomplicated abscesses [1, 21]. In a randomized placebo-controlled trial involving 780 patients across 6 centers, Daum et al. demonstrated that in cases of MRSA, even abscesses smaller than 5 cm saw a greater than 20% improvement in cure rate with the addition of oral antibiotics to incision and drainage [1]. This study was included in a meta-analysis of 2400 patients which concluded that the addition of adjunctive systemic antibiotics directed toward MRSA improved cure rates of the primary abscess after incision and drainage and also reduced the rate of recurrence [21]. The decision to treat with adjunctive antibiotics should always take into account the immune status of the patient, risk versus benefit of antibiotics, and the extent of the infectious process (e.g., surrounding cellulitis, number of abscesses).

Several non-beta-lactam oral antibiotics for the empirical treatment of CA-MRSA SSTIs have been recommended. Of these, clindamycin and trimethoprim-sulfamethoxazole are the most studied due to their availability, tolerance, cost, and in vitro activity against MRSA and MSSA [5]. In multiple head-to-head studies, both drugs were found to have equal efficacy in terms of treatment success of SSTIs, including

abscesses. Interestingly, some of these studies demonstrated less recurrent infection with clindamycin compared to trimethoprim-sulfamethoxazole [1, 2, 8]. The choice of empirical antibiotic should be guided by local MRSA susceptibilities, drug interactions, and patient allergies/comorbidities (Table 19.1).

In patients with extensive infection or signs of systemic inflammatory response, admission for parenteral antibiotics may be warranted. In these cases, the IDSA recommends treatment with either vancomycin, linezolid, daptomycin, or clindamycin [20]. Caution should be used when choosing

Table 19.1 Oral antibiotic choices for empiric treatment of MRSA skin infections

| Antibiotic | Dose | Potential adverse effects |
|---|---|---|
| Clindamycin | 300–450 mg three times a day[a] | Diarrhea, GI upset, increased incidence of *Clostridioides difficile* infection |
| Trimethoprim-sulfamethoxazole | 1–2 DS twice a day[a] | Nausea, rash, hyperkalemia, mild artificial increase in serum creatinine, acute kidney injury, teratogenic in the third trimester |
| Doxycycline | 100 mg twice a day[a] | Photosensitivity, nausea, vomiting, avoid in pregnant women and children |
| Minocycline | 100 mg twice a day[a] | Nausea, vertigo, photosensitivity, avoid in pregnant women and children, and renal insufficiency |
| Linezolid | 600 mg twice a day[a] | Costly, potential for bone marrow suppression, increased risk of serotonin syndrome, GI upset |

Liu et al. [20]

[a]Duration 5–10 days, based on clinical response

clindamycin for severe MRSA infections due to the rising prevalence of inherent and inducible resistance [22]. Ceftaroline, a parenteral fifth-generation cephalosporin with activity against MRSA, has also been approved by the FDA for the treatment of SSTI due to MRSA. Studies have demonstrated that ceftaroline was non-inferior to vancomycin IV plus aztreonam for MRSA skin infections including abscesses [11, 23].

## *Risk Factors for Infection*

Several risk factors have been associated with MRSA skin infection including recent exposure to antibiotics, MRSA colonization, and history of previous MRSA infection. Known colonization sites include the anterior nasal pharynx, axilla, and groin [2, 7, 15, 24–27], and colonization (intermittent or permanent) rates are as high as 50–60%. Review of the data has demonstrated a high specificity for a positive MRSA screen and MRSA SSTI, especially in cases in abscesses [26, 27]. Epidemiological studies have also identified certain populations at increased risk including athletic teams, military personnel, and incarcerated individuals. Though MRSA skin infections have been identified in a multitude of sports of varying levels, most studies on MRSA infections related to sports participation have focused on football [28]. In 2003, the CDC investigated an outbreak of MRSA skin infections among the St. Louis Rams professional football team. They found that MRSA skin infections largely manifested as abscesses and were associated with uncovered skin abrasions. The most frequently affected players were those whose position resulted in the most frequent person-to-person contact. After the institution of several infection control measures including access to chlorhexidine containing hand soap dispensers and appropriate local wound care, incidence of MRSA skin infections drastically dropped the following season [29].

## *Recurrent Infection and the Role of Decolonization*

Unfortunately, the rate of recurrent skin and soft tissue infections due to MRSA remains high, with upward of 50% of patients experiencing a repeat episode within 1 year [2, 7]. Despite the association between MRSA colonization and MRSI SSTIs, the role of decolonization in primary and recurrent MRSA SSTI prevention remains to be defined. Multiple decolonization strategies have been suggested from topical treatment with nasal mupirocin and chlorhexidine/bleach baths to systemic oral antibiotics, or a combination of the three. A Cochrane review in 2003 demonstrated no difference in rates of decolonization between these regimens compared to no treatment [9]. It appears that recolonization by MRSA occurs within months of successful decolonization. In addition, decolonization efforts have led to increasing rates of resistance to decolonization agents such as mupirocin. Regardless, several small studies have demonstrated a reduction in recurrent MRSA SSTI rates after decolonization efforts. Based on these studies, the IDSA recommends considering MRSA decolonization in patients with recurrent MRSA skin and soft tissue infections but notes the duration of such treatments is unknown [20] (Table 19.2).

## *Differential Diagnoses*

When managing patients with suspected CA-MRSA skin and soft tissue infections, it is important to be aware of various conditions that may present similarly to cutaneous abscesses. For example, hidradenitis suppurativa, an inflammatory skin condition associated with deep-seated painful nodules, may also present with what initially appear to be recurrent skin "abscesses." The lesions of hidradenitis suppurativa, which include scarring and sinus tracts, occur characteristically in the apocrine gland-bearing regions: the axilla, groin, buttocks, and inframammary folds [27, 28]. Patients with hidradenitis suppu-

Table 19.2 Suggested regimens for decolonization of MRSA[1]

| |
|---|
| Nasal decolonization |
| Topical mupirocin applied twice daily for 5–10 days |
| Skin decolonization |
| Application of antiseptic solution, such as chlorhexidine, daily for 5–14 days<br>or<br>Dilute bleach bath (1 teaspoon of bleach per gallon of water) for 15 minutes twice weekly for 3 months |
| Systemic antibiotics are not recommended as part of routine decolonization |

IDSA: Clinical Practice Guidelines by the Infectious Diseases Society of America for the Treatment of Methicillin-Resistant Staphylococcus aureus Infections in Adults and Children 2011

rativa are distinguished by the chronic and recurrent nature of these nodules in these typical regions. Interestingly, microbiological studies of these lesions are frequently negative or demonstrate typical skin flora, and management of severe disease is focused on immunomodulatory therapy and surgical excision, rather than prolonged antibiotic therapy [30–32]. Inflamed epidermoid cysts may also present similarly to a skin abscess with tenderness, erythema, and a fluctuant nodule. Unlike an abscess, the inflammation is due to rupture of the cystic contents into the surrounding dermis rather than infection [8].

Many patients who present with a CA-MRSA abscess often report a spider bite as the initial insult leading to the development of the skin lesion [16]. In one particular study, 182 patients presented to an emergency department with a complaint of a "spider bite," and only 7 patients (3.8%) were diagnosed with spider bites, while 156 patients were diagnosed with infection; two-thirds of those were secondary to CA-MRSA [33]. The spider that is most commonly implicated is the brown recluse spider (*Loxosceles reclusa)*, even in areas of the country where they do not exist. Patients must be educated regarding the native range of this spider (south and central midwestern USA) as well as differentiating clinical characteristics associated with CA-MRSA skin infections and spider bites.

**Clinical Pearls**

1. The mainstay of treatment for MRSA abscesses is incision and drainage of the lesion.
2. The addition of oral antibiotics for 5–10 days with empirical coverage of CA-MRSA is beneficial after I&D in some situations. Oral antibiotics include clindamycin, trimethoprim-sulfamethoxazole, tetracyclines, and linezolid.
3. Recurrent MRSA skin/soft tissue infections are common.
4. MRSA decolonization is recommended for recurrent SSTIs, but benefit and optimal regimen remains unclear.

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# Chapter 20
# Vertebral Osteomyelitis and Discitis

**Rick Placide**

## Case 1

A 48-year-old female presents with approximately 3 months of atraumatic, progressive neck and shoulder pain and diffuse myalgias. Subjectively, she complains of intermittent fevers but no other constitutional signs or symptoms. She denies upper or lower extremity neurological symptoms. Her past medical history includes intravenous drug abuse, methicillin-resistant *Staphylococcus aureus* bacteremia, and anxiety. Work-up including imaging of the cervical spine (Figs. 20.1 and 20.2) demonstrates osteomyelitis/discitis at C6, 7 and an epidural abscess in the cervical spine. The patient underwent anterior cervical corpectomy C6, 7 and spinal reconstruction C5-T1. Operative cultures grew *Klebsiella pneumoniae*.

## Case 2

A 69-year-old female visiting family in the United States from South America presents with 3 months of insidious mid-thoracic back pain followed by 2 weeks of progressive lower

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J. Reznicek et al. (eds.), *Musculoskeletal Infections*,
https://doi.org/10.1007/978-3-030-41150-3_20

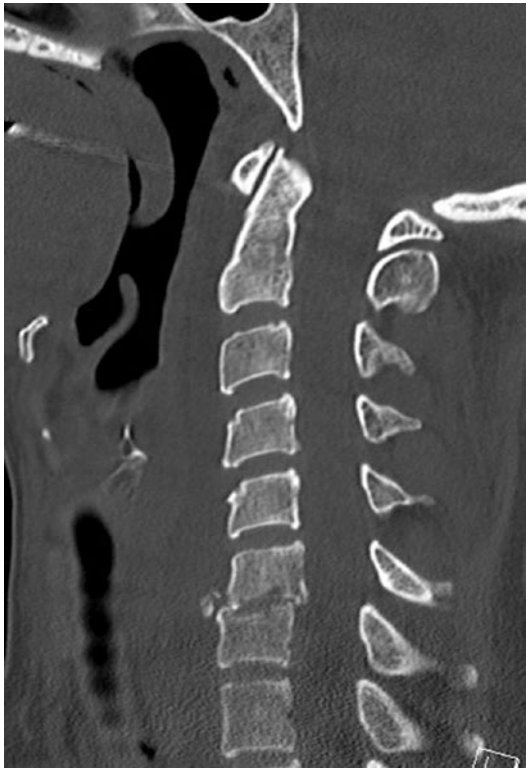

FIGURE 20.1 Sagittal CT of the cervical spine demonstrating destructive changes at the C6–7 disc space and adjacent vertebral body endplates

extremity weakness and numbness. At the time of presentation, she was unable to ambulate secondary to the lower extremity weakness. She denies any recent injuries to the back or any constitutional signs or symptoms. Past medical history includes high blood pressure and a cardiac arrhythmia. She has a history of lumbar spine surgery. Work-up including imaging (Figs. 20.3 and 20.4) demonstrated osteomyelitis/discitis T6, 7, 8 and epidural phlegmon with cord compression T7, 8. The patient underwent posterior corpec-

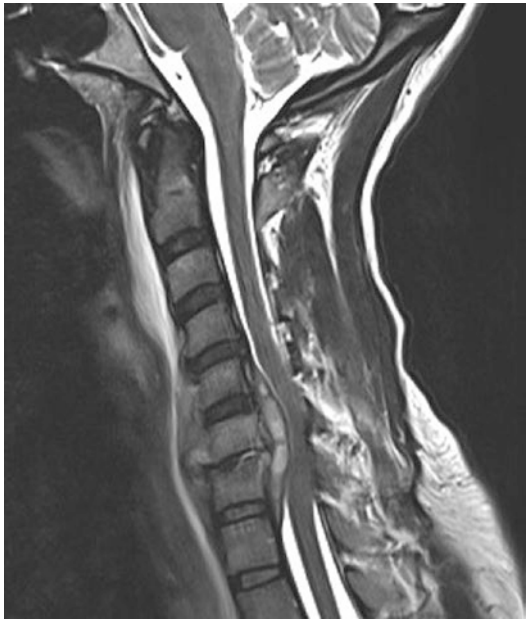

FIGURE 20.2 Sagittal T2-weighted MRI demonstrating epidural abscess with spinal cord compression C5-T1

tomy T6–8 and spinal reconstruction T3–T11. Operative cultures grew carbapenem-resistant *Pseudomonas aeruginosa*. She was subsequently transferred to inpatient rehabilitation, and at the time she returned to her hometown in South America, she was ambulating with a walker and her preoperative thoracic back pain had resolved.

## Discussion

Spinal infections account for 2–7% of orthopedic infections [1]. In developed countries, the incidence can range from 1:100,000 to 1:250,000 [2]. The incidence has been increasing in recent decades, partly related to an increase in immunocompromised patients, aging of the population, improved

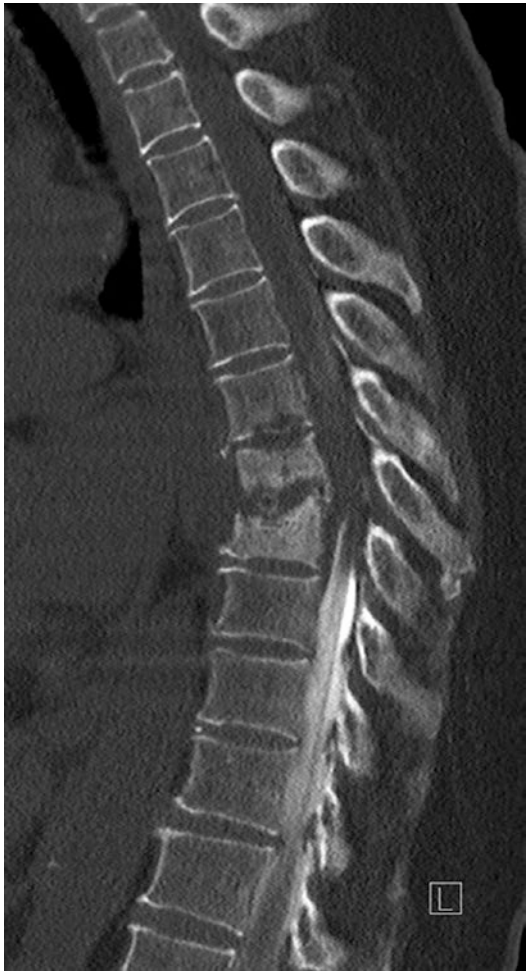

FIGURE 20.3 Sagittal CT myelogram demonstrating destructive changes at T6, 7, 8

diagnostic capabilities, and, more recently, increased intravenous drug abuse [3]. Spinal infections can be caused by bacteria, fungi, mycobacteria, and parasites. While bacteria are overall the most common offending organism, regional variations exist. For example, in areas where tuberculosis is

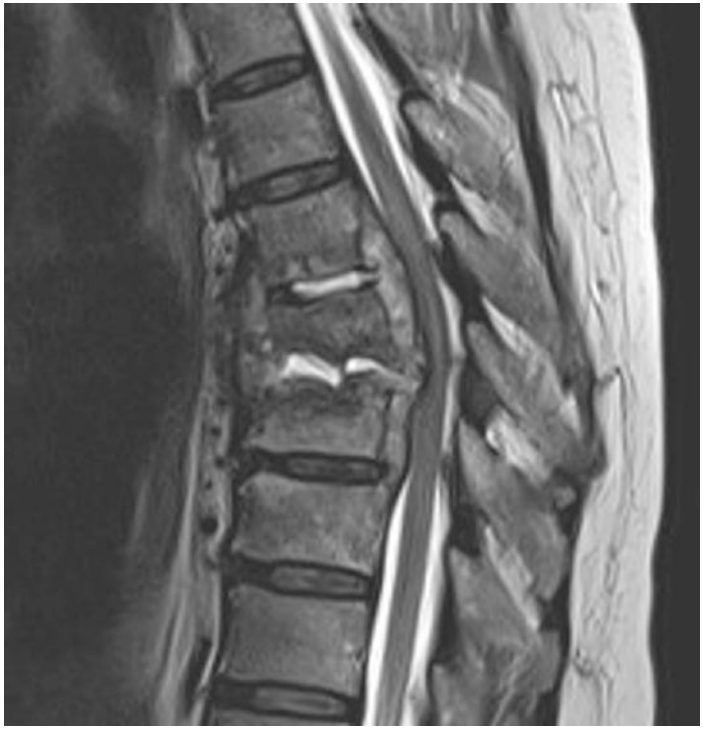

FIGURE 20.4 Sagittal T2-weighted MRI demonstrating bony destructive changes at T6, 7, 8, increased signal in the T6–7, 7–8 disc spaces, kyphotic deformity, and epidural phlegmon with spinal cord compression

endemic, tubercular spinal infection (Pott's disease) can be a significant source of spinal pathology.

Spinal infections are typically described by the anatomical location of the infection. Discitis refers to an infection in the intervertebral disc space, more common in children. Osteomyelitis is an infection in the vertebra, most commonly the vertebral body. Epidural abscess is an infection in the epidural space. Less commonly, infection can be found in the facet joints (septic arthritis), paraspinal soft tissues (psoas muscle, retropharyngeal space), and subdural/subarachnoid space. Vertebral body osteomyelitis and discitis are generally

seen together on imaging, often referred to as pyogenic spondylodiscitis, and this is the most common type of infection encountered in the spine. The lumbar spine is most often involved, followed by the thoracic and then cervical spine [4].

Infection is thought to access the spine by one of three mechanisms. Hematogenous spread from a remote infected site to the spine is the most common (*Staphylococcus* from a skin infection, *Escherichia coli* from a urinary tract infection, *Streptococcus* from an infected heart valve). Spread to the spine from an adjacent infection and direct inoculation (e.g., postsurgical) are the other two mechanisms. *Staphylococcus aureus* is the most common causative organism and is typically a monomicrobial infection [2]. Gram-negative organisms can account for up to 25% of spinal infections, and polymicrobial spinal infections range from 10% to 20% [5].

It is not uncommon to have a delay in the diagnosis of a spinal infection [6]. The most common chief complaint in patients with a spinal infection is neck or back pain of insidious onset, and this is present in approximately 90% of patients. Most patients present about 1–2 months after the onset of symptoms. Low-grade fever is present in about 65% of patients and neurological deficit is initially noted in 5–30% [7]. Occasionally, a patient will present with signs and symptoms of sepsis. A delay in diagnosis has been shown to increase morbidity and mortality; however, recognizing risk factors can help prevent diagnostic delay. Comorbidities that predispose to a spinal infection include older age, diabetes mellitus, IV drug abuse, immune system compromise, alcoholism, liver disease, end-stage renal disease, obesity, and a previous spinal procedure/surgery [8]. Since most de novo spinal infections occur due to hematogenous spread from infection elsewhere, a complete history and physical exam may help identify the source of the infection. Up to 30% of patients with a de novo spinal infection will also have infection of the heart valves and endocardium [9].

Additional work-up should include laboratory blood tests (complete blood count, metabolic profile, erythrocyte sedimentation rate, c-reactive protein and blood cultures). If the clinical situation permits, it is recommended to hold antibiotics until cultures have been obtained. If the patient is systemically ill, broad-spectrum intravenous antibiotics should be initiated. Appropriate imaging is critical to the diagnosis and management of a spinal infection. While magnetic resonance imaging (MRI) is the imaging modality of choice for spinal infections, plain radiographs and computed tomography (CT) scans have a role. MRI scans should be obtained of the entire spinal axis due to the possibility of skip lesions [10]. Due to the potential for significant morbidity and mortality, patients with a spinal infection should be managed at a center with specialists in critical care, internal medicine, infectious diseases, and spine surgery. In cases involving neurological deficits, rehabilitation specialists should be involved as well.

If blood cultures are positive and imaging suggests a spinal infection, antibiotic treatment can be initiated based on the blood cultures. When blood cultures are negative, percutaneous aspiration/biopsy of the infected site is warranted. However, recent data suggest the diagnostic yield for CT-guided biopsies in cases of suspected spinal infection is about 33% [11]. When blood cultures and percutaneous biopsies are negative, open surgical biopsy is recommended. Typically, tissue cultures are tested for aerobic, anaerobic, and fungal pathogens, as well as acid-fast bacilli. Non-operative treatment of patients with a spinal infection includes antibiotics, bracing, and close follow-up. In the case of neurological deficits, bony destruction causing spinal instability/deformity or intractable pain, or failure of a course of IV antibiotics and bracing, surgical debridement, and spinal reconstruction, deserves strong consideration [12, 13]. When considering the timing of surgery for spinal infection, patients having early surgery have better outcomes than those having their surgery delayed [14].

**Clinical Pearls**

1. The incidence of spinal infections has increased in recent decades, and these infections have the potential to result in significant morbidity and mortality.
2. A delay in diagnosis of a spinal infection is not uncommon and can lead to poor outcomes. A high index of suspicion and recognition of risk factors for spinal infection is critical to avoid diagnostic delay.
3. Many cases of spinal infection can be managed with antibiotics and bracing. Operative intervention becomes necessary in cases of failed nonoperative management, need for an open biopsy, and spinal instability and/or neurologic deficit.
4. Spinal infections are best managed with a multidisciplinary approach, including internal medicine, infectious diseases, and spine surgery.

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J. Reznicek et al. (eds.), *Musculoskeletal Infections*,
https://doi.org/10.1007/978-3-030-41150-3